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SELECTED ABSTRACTS ON ANIMAL MODELS
FOR BIOMEDICAL RESEARCH

Charles B. Frank, et al

National Academy of Sciences-National Research
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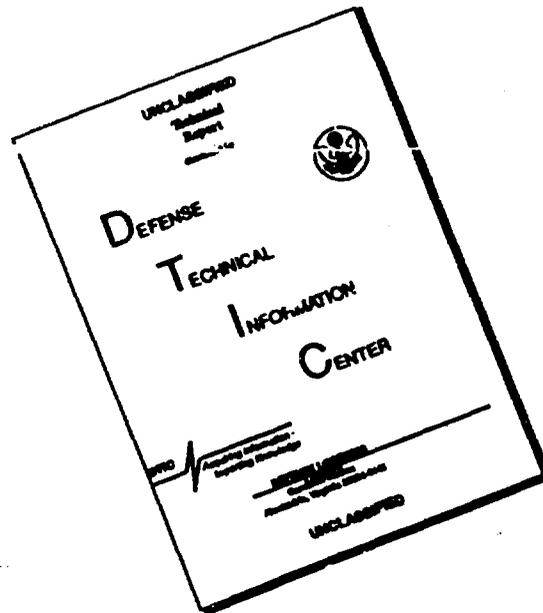
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SELECTED ABSTRACTS

ON

ANIMAL MODELS FOR

BIOMEDICAL RESEARCH

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INSTITUTE OF LABORATORY ANIMAL RESOURCES

The Institute of Laboratory Animal Resources (ILAR) was founded in 1952 within the Division of Biology and Agriculture. It serves as a coordinating agency to disseminate information, survey existing and required resources, establish standards, promote education, hold conferences, and generally to upgrade laboratory animal resources.

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PREFACE

The Animal Models and Genetic Stocks Program is an information exchange service conducted by the Institute of Laboratory Animal Resources (ILAR). This program was initiated in July 1969 as a result of resolutions adopted by the Genetics Society of America and the National Institutes of Health. These resolutions cited the urgent need to establish a central agency to collect, maintain, and disseminate information on vertebrate models and genetic stocks useful for biomedical research. The objectives of the program are to inform the biomedical community of the various animal models for research and to provide information that will assist scientists in selecting and locating a particular species or strain of animal to serve as a model.

It was with these objectives in mind that the Committee on Animal Models and Genetic Stocks and its supporting staff selected from more extensive files the abstracts contained in this publication. The abstracts were compiled and edited by Dr. Charles B. Frank, Staff Officer, and Miss Marilyn J. Anderson, Research Assistant. It is hoped that these abstracts will be of value to biomedical investigators.

The information accumulated within the program includes selected key references describing animal models, sources of supply and characteristics of these animals, and the names of people who may serve as consultants or as sources of additional information on a particular animal model or genetic stock. Data are made available without charge to interested individuals through periodic publications and by response to specific inquiries.

Information is continuously collected on colonies of animals that can serve as models for biomedical research. ILAR is asking investigators to assist in the development of its data bank by providing information on animal models or genetic stocks maintained within their institutions. A sample colony data form appears on page 43. Your cooperation in completing this form and providing the information to ILAR will aid in the further development of the Animal Models and Genetic Stocks Information Exchange Program.

ILAR believes this to be an important program with great potential for improving communication within the biomedical community. However, the support of every investigator is essential if a comprehensive listing of the animal models and genetic stocks being used throughout the country is to be maintained. Interested persons are urged to make suggestions regarding the program and to furnish all information they may have concerning potential models or genetic stocks. Readers are requested to complete and return the questionnaire on page 45 to assist ILAR in evaluation of this publication. Correspondence should be addressed to:

Animal Models and Genetic Stocks Program
Institute of Laboratory Animal Resources
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SELECTED ABSTRACTS ON ANIMAL MODELS FOR BIOMEDICAL RESEARCH

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GENERAL REFERENCES

1. Homburger, F. (9 Commercial Avenue, Cambridge, Massachusetts 02141), and E. Bajusz. 1970. New models of human disease in Syrian hamsters. J. Amer. Med. Assn. 212:604-610.

The resemblance of 5 new constitutional (hereditary) diseases in inbred Syrian hamsters (muscular dystrophy, cardiomyopathy with congestive heart failure, obesity, adrenal adenomatosis, and progressive hind-leg paralysis) to human disease entities makes these animals useful for systematic experimental study. The hamsters have also demonstrated peculiar inherited susceptibilities to teratogenic agents (thalidomide), poisoning by cyclamates through coronary and systemic calcinosis, and the carcinogenic activity of polycyclic hydrocarbons. - *Authors' abstract.*

2. Potkay, S. (U. S. Department of Health, Education and Welfare, Public Health Service, National Institutes of Health, Division of Research Service, Laboratory Aids Branch, Bethesda, Maryland 20014). 1970. Diseases of the opossum (*Didelphis marsupialis*): A review. Lab. Anim. Care 20:502-511.

The opossum (*Didelphis marsupialis*) is being utilized as a research animal with increasing frequency. The naturally occurring and experimentally induced diseases that affect this species have been reviewed. They include rabies, pseudorabies, B virus infection, tuberculosis, tularemia, leptospirosis, relapsing fever, streptococcal infections, and endemic murine typhus. The opossum is the host for numerous parasites. Helminths are most commonly encountered, and a number of ectoparasites are associated with the opossum. *D. marsupialis* serves as a reservoir for Chagas' disease and is also susceptible to other protozoan infections. Histoplasmosis occurs in opossums, and dermatophytes have been isolated from this species. Diseases such as rickets, nephritis, pneumonia, hepatitis, and various neoplasms also afflict the opossum. All of the reported diseases should be considered important, particularly in opossums that are obtained directly from the wild for use in research. - *Author's summary.*

ALIMENTARY SYSTEM

3. Allen, J. R. (University of Wisconsin, 470 N. Charter Street, Madison, Wisconsin 53706), and L. A. Carstens. 1971. Monocrotaline-induced Budd-Chiari syndrome in monkeys. Amer. J. Dig. Dis. 16:111-121.

Budd-Chiari syndrome was produced in adult *Macaca speciosa* monkeys within 3 months by the parenteral administration of the pyrrolizidine alkaloid monocrotaline. These animals developed ascites, distended abdominal veins, hypoproteinemia, and an increase in portal venous pressure. The vascular lesions included partial to

complete occlusion of hepatic veins throughout the liver. These venous alterations were initiated by endothelial lysis. As a result of the altered permeability, blood components collected throughout the vessel wall, producing marked disruption. Occlusion of the affected vessels followed the encroachment of the thickened edematous wall on the lumen. Eventually these hepatic veins underwent fibrous connective tissue repair, giving rise to widespread focal fibrosis throughout the livers. - *Authors' abstract.*

4. Cornelius, C. E. (Department of Physiological Sciences, College of Veterinary Medicine, Kansas State University, Manhattan, Kansas 66502). 1970. Dubin-Johnson syndrome. *Comp. Pathol. Bull.* 2(3):2.

The biologic features and pathologic findings of the Dubin-Johnson Syndrome in Corriedale sheep are described. The black livers of mutant Corriedale sheep with this syndrome appear functionally and morphologically identical to those observed in the human counterpart disease. The syndrome in the ovine mutant is unlike that in man in being lethal under field conditions because of the complication of photosensitivity from the ingestion of chlorophyll in green feed. Nevertheless, Corriedale sheep appear to be a useful animal model for the study of Dubin-Johnson Syndrome or congenital hyperbilirubinemia in man. - *M.J.A.*

5. Dreizen, S. (University of Texas Dental Science Institute, P.O. Box 20068, Houston, Texas 77025), and B. M. Levy. 1969. Histopathology of experimentally induced nutritional deficiency cheilosis in the marmoset (*Callithrix jacchus*). *Arch. Oral Biol.* 14:577-582.

A folic acid deficiency syndrome closely resembling the human counterpart has been produced experimentally in cotton ear marmosets (*Callithrix jacchus*) restricted to a folic acid-free purified diet. Intramuscular injections of the folic acid antagonist, methotrexate, speeded and intensified the onset and emergence of the deficiency disease in animals so treated. Eight of the 15 marmosets developed bilateral angular cheilosis as part of the syndrome. The angular stomatitis followed a clinical course similar to human nutritional deficiency cheilosis. The lesions were characterized histologically by a degeneration and superimposed inflammation of the labial commissures starting at the mucocutaneous junction and sequentially penetrating the epithelial, connective tissue and muscle layers. - *Authors' summary.*

6. Lorenz, D. (Division of Biologics Standards, National Institutes of Health, Bethesda, Maryland 20014), L. Barker, D. Stevens, M. Peterson, and R. Kirschstein. 1970. Hepatitis in the marmoset, *Saguinus mystax*. *Proc. Soc. Exp. Biol. Med.* 135:348-354.

The marmoset, *Saguinus mystax*, developed signs of disease similar to human hepatitis when inoculated with marmoset sera containing Deinhardt's hepatitis agent, or sera from patients with infectious hepatitis but not when inoculated with serum containing hepatitis-associated antigen or with partially purified antigen. The evidence of disease were 3- to 10-fold increase above normal SGPT

levels and histologic changes of single liver cell necroses with periportal lymphocytic infiltration. Hepatitis-associated antigen was not found in any marmoset sera by complement-fixation tests or electron microscopy. - *Authors' summary.*

7. Madden, J. W. (Department of Surgery, University of Arizona, College of Medicine, Tucson, Arizona 85721), P. M. Gertman, and E. E. Peacock, Jr. 1970. Dimethylnitrosamine-induced hepatic cirrhosis: A new canine model of an ancient human disease. *Surgery* 68:260-268.

A new canine model of hepatic cirrhosis, created by intermittent, oral administration of dimethylnitrosamine, a specific hepatotoxin, is described. DMNA-induced cirrhosis is stable or progressive after discontinuing the toxin, is associated with significant physiological abnormalities which correlate with severity of histological lesions, and can be produced rapidly. Histological, biochemical, and physiological abnormalities associated with DMNA-induced cirrhosis resemble many features of hepatic cirrhosis in man. Data suggest that this model may be useful in studying other parameters of this complex disorder. - *Authors' summary.*

8. Okabe, S. (Institute of Gastroenterology, Presbyterian-University of Pennsylvania Medical Center, 51 N. 39th Street, Philadelphia, Pennsylvania 19104), J. L. A. Roth, and C. J. Pfeiffer. 1971. Differential healing periods of the acetic acid ulcer model in rats and cats. *Experientia* 27:146-148.

It is known that submucosal injection of several agents, including silver nitrate, formalin, nicotine, and epinephrine, can induce gastric ulcers in experimental cats and dogs. These experimental lesions grossly and histologically resemble human gastric ulcers, although they heal rapidly in 2-3 weeks. In a previous study, a chronic ulcer model in rats was developed that requires the gastric submucosal injection of acetic acid and produces an ulcer that persists for 150 days. The purpose of the present study was to test the acetic acid ulcer procedure in cats, in which the gross anatomy of the stomach is similar to that of man, and to compare the healing periods with those in the rat. It is concluded that the chronicity of the gastric ulcer in the rat is not necessarily related to the acetic acid itself, but to a special characteristic of the rat. Furthermore, inasmuch as the chronicity of the experimental acetic acid ulcer model in the rat uniquely resembles human peptic ulcer, this model may be quite useful for the study of human ulcer and the evaluation of pharmacologic agents used for this disease. -*M.J.A.*

9. Porta, E. A. (The Research Institute of the Hospital for Sick Children, Toronto 2, Canada), O. R. Koch, and W. S. Hartroft. 1969. A new experimental approach in the study of chronic alcoholism. IV. Reproduction of alcoholic cirrhosis in rats and the role of lipotropes versus vitamins. *Lab. Invest.* 20:562-572.

Alcoholic cirrhosis has never been reproduced in experimental animals consuming, along with ethanol, adequate or even inadequate basal diets. However,

in this study using the procedure of giving sweetened alcohol to rats consuming separately an originally adequate basal diet, it was possible to create in the final dietary regimen (alcohol plus food) inadequacies capable of severely injuring the liver. Fatty livers, hepatofibrosis, cirrhosis, and Mallory bodies have now been reproduced in rats by this approach. It was found that the deficiency of lipotropes induced by either alcohol or sucrose was more important than deficiency of vitamins, similarly induced, in the development of these changes. These results also provide evidence that the consumption of appreciable amounts of alcohol by rats for periods as long as 7 months will not produce liver damage in rats given adequate dietary protection. However, the degree of Mallory body formation was inversely related to the alcohol- or sucrose-induced deficiencies of lipotropes and vitamins. The authors conclude that the combination of the consumption of alcohol, at the level of 37% of the total calories, plus the unsupplemented basal diet reported in this study, provides a model for the duplication in rats of "alcoholic cirrhosis" in man. - *Authors' abstract modified.*

10. Sethbhakdi, S., C. J. Pfeiffer (Institute of Gastroenterology, Presbyterian-University of Pennsylvania Medical Center, 51 N. 39th Street, Philadelphia, Pennsylvania 19104), and J. L. A. Roth. 1970. Gastric mucosal ulceration following vasoactive agents. A new experimental model. Amer. J. Dig. Dis. 15:261-270.

The influence of the vasoactive catecholamines, epinephrine and norepinephrine, has been investigated in regard to the comparative ulcerogenicity on the gastric glandular mucosa of the rat. The unique extensive, hemorrhagic necrosis, and ulcerations which appear in the fundus--but not the antrum--following single injections of these drugs are readily quantified because of the continuous nature of the lesion. A standard assay has been developed with this new ulcer model, which results in extensive mucosal ulceration (43% of fundus with lesions) in 100% of treated animals after only 5 hours. The optimal procedure requires the single intraperitoneal epinephrine injection of 0.4 mg/kg to young adult Sprague-Dawley rats 4 hours after pylorus occlusion, and the sacrifice of animals 1 hour after injection. This experimental gastric lesion is dependent upon the presence of gastric acid, and is completely inhibited by bilateral vagotomy, and almost completely inhibited by the presence of a magnesium-aluminum hydroxide gel-type antacid. - *Authors' abstract.*

11. Terblanche, J. (The Liver Research Group, Department of Surgery, University of Cape Town, Cape Town, South Africa), R. Hickman, D. M. Dent, H. Spilg, G. G. Harrison, and S. J. Saunders. 1970. The use of domestic pigs in medical research in South Africa.
 1. Liver and anaesthetic research. J. South Afr. Vet. Med. Assn. 41:93-103.

Results of a study of the pig as an experimental model for liver homotransplantation are presented. The problem of gastric ulceration in pigs with liver transplants is discussed, and a solution to the problem is presented. Reference is made to the increasing volume of veterinary literature on the problem of gastric ulceration in pigs. Malignant hyperpyrexia, which is a recently

recognised hazard of anaesthesia in man, has been demonstrated to occur in 25% of a group of Landrace pigs in the Western Cape. The use of the pig liver in an isolated perfusion circuit to study liver physiology, and to attain storage for liver transplantation is presented. The pig's liver in a similar circuit has also been used to treat patients with fulminating liver failure. - *Authors' summary modified.*

12. Wanke, M. (Institute of Pathology, University of Heidelberg, Heidelberg, West Germany). 1970. Experimental acute pancreatitis. *Curr. Topics Pathol.* 52:65-142. (463 refs.)

This monograph on experimental acute pancreatitis reviews the history of experimental pancreas research and the anatomical, physiological, and biochemical premises of such work. The authors discuss comparative studies and the application of experimental results to conditions in man, and it is emphasized that the different enzyme patterns in related species and species-specific anatomical features are important. Sections on spontaneous pancreatitis in animals, theories on the development of pancreatitis, and experimental models are presented. The morphological and biochemical substrates of various models are reviewed, including bile, elastase, trypsin/chymotrypsin, lipase, and acids. The paper represents a comprehensive overview of the research in experimental pancreatitis with particular reference to the various animal models utilized in this field. - *M.J.A.*

13. Yasin, R. L (Chester Beatty Research Institute, Institute of Cancer Research, Royal Cancer Hospital, Fulham Road, London S. W. 3), and C. L. Leese. 1970. The production of chronic gastritis and ulceration in the glandular stomach of rats by iodoacetamide (IAM). *Europ. J. Cancer* 6:425-432.

Iodoacetamide consistently produced chronic gastritis and ulceration, the initial effect being the production of diffuse hyperemia, focal necrosis and other abnormalities in the mucosal epithelium. With continued treatment ulceration of the body mucosa became extensive and chronic gastritis ensued. Pyloric and duodenal epithelium exhibited disturbances in proliferation kinetics. Gastric juice volume, acid and pepsin output were consistently increased in treated animals, suggesting that the rate of secretion is not inhibited by iodoacetamide despite the presence of extensive ulceration but that modification of some normal control mechanisms occurs. Ulceration and gastritis is considered to arise through damage to the mucosal barrier by iodoacetamide thereby lowering the resistance of the mucosal epithelium to proteolysis; recurrent damage producing chronic gastritis. The gastritis lesions observed in this study have many similarities to those seen in the corresponding human disease. - *Authors' summary modified.*

CARDIOVASCULAR SYSTEM

14. Besterman, E. M. M. (Cardiology Department, St. Mary's Hospital, London W. 2, Great Britain). 1970. Experimental coronary atherosclerosis in rabbits. *Atherosclerosis* 12:75-83.

Intermittent cholesterol feeding of mature rabbits for periods of 6-30 months has produced atherosclerotic lesions of the main coronary arteries apparently similar to those found in man. The advantages of the rabbit as an experimental animal are stressed. Individual variations in response to cholesterol feeding were observed. - *Author's summary.*

15. David, M. S. (Division of Cardiovascular and Thoracic Surgery, Queen's University, Kingston, Ontario, Canada), E. J. P. Charrette, and R. R. Lynn. 1970. Experimental coronary artery thrombosis for production of cardiogenic shock. *Canad. J. Surg.* 13:189-194.

A model has been devised for the production of cardiogenic shock in the closed chest dog. In almost every instance, stable but subnormal cardiac function can be produced after proximal coronary artery thrombosis. By employing proximal coronary artery obstruction in the closed chest animal, a situation is produced that closely resembles coronary thrombosis in humans. This model should permit satisfactory studies of mechanical supportive measures aimed at increasing coronary artery flow and stimulating the development of inter-coronary anastomoses. - *Authors' summary.*

16. Ehrlich, F. E. (Surgical Research Laboratory of the United States Naval Hospital, Chelsea, Massachusetts), S. G. Kramer, and E. Watkins, Jr. 1969. An experimental shock model simulating clinical hemorrhagic shock. *Surg. Gynecol. Obstet.* 129:1173-1180.

A reproducible, single model for the study of hemorrhagic shock in the dog is based on the withdrawal of 42% of the blood volume in the dog, as measured by a ten minute dilution of ¹³¹I albumin, at a precise rate during a ten minute period. Physiologic and biochemical alterations in ten dogs which underwent splenectomy and were subjected to this protocol were measured. The alterations in arterial pressure, pulse rate, venous pressure, respiratory rate, arterial pH, arterial pO₂ and pCO₂, venous lactate concentrations, and blood volume were all in keeping with the clinical picture of hemorrhagic shock as seen in human. The rather marked clinical correlation of the model would seem to make it useful in studying new therapeutic methods. - *Authors' summary modified.*

17. Elzinga, W. E. (Cardiovascular Physiology Laboratory, Hittman Associates, Incorporated, Columbia, Maryland 21043). 1969. Experimental myocardial infarction--An animal model. *Bull. Pathol.* 10:402, 426.

The development of an animal model that mimics human myocardial infarction is reported in dogs and calves. The animal model developed appears to simulate human myocardial infarction in many respects. The vessel is damaged at the site of attachment of the thrombus; enzyme activity (LDH, SGOT, and CPK) is increased; cardiac arrhythmias are induced; electrocardiographic changes during myocardial ischemia, injury, and infarction resemble those seen in man; and secondary vessels are often occluded, as a result of embolism from the primary thrombus. - *Author's summary modified.*

18. Garrison, P. K. (Department of Medicine and Pediatrics, Yale-New Haven Hospital, New Haven, Connecticut), and L. R. Freedman. 1970. Experimental endocarditis. I. Staphylococcal endocarditis in rabbits resulting from placement of a polyethylene catheter in the right side of the heart. Yale J. Biol. Med. 42:394-409.

Polyethylene catheters with their tips at the entrance to or within the right side of the heart produce sterile marantic endocarditis and tricuspid valvulitis. Introducing as few as 10^2 microorganisms within the catheter predictably produced staphylococcal endocarditis. The course of the disease was variable, some animals surviving for six weeks. The technique was simple and did not require hemodynamic, immunologic or endocrine manipulations of the animals. Splenomegaly was frequently found in association with endocarditis but positive blood cultures were inconstant. Kidney infections were observed but there were no examples of proliferative glomerulonephritis. This model is suitable for the study of the bacteriologic, pathologic, and immunologic aspects of bacterial endocarditis and reproduces some of the complications of indwelling venous catheterization that have been observed in man. - *Authors' summary modified.*

19. Mohiuddin, S. M. (Institut de Cardiologie de Quebec, Laval University, Quebec, Canada), P. K. Taskar, M. Rheault, P. E. Roy, J. Chenard, and Y. Morin. 1970. Experimental cobalt cardiomyopathy. Amer. Heart J. 80:532-543.

An animal model for cobalt-induced cardiac disease is reported. Cardiac lesions involving the pericardium, the myocardium, and the endocardium were produced in guinea pigs by oral administration of 20 mg. per kilogram per day of cobalt. Light and electron-microscopic features and electrocardiographic findings of experimentally produced cobalt lesions were strikingly similar to those observed in Quebec beer drinkers' cardiomyopathy. Addition of 2 Gm. of ethyl alcohol to the cobalt regimen failed to modify the incidence or the severity of the disease. - *Authors' summary.*

20. Ratliff, N. B. (Department of Pathology, Duke University Medical Center, Durham, North Carolina 27706), R. H. Peter. B. W. Ramo, W. R. Somers, and J. J. Morris. 1970. A model for the production of right ventricular infarction. Amer. J. Pathol. 58:471-474.

Experimental right ventricular hypertrophy increases the susceptibility of the right ventricular myocardium to infarction following gradual right coronary occlusion in farm pigs. The model presented provides a vehicle for the investigation of some of the factors (pressure and mass) which may affect the susceptibility of the ventricle to infarction. - *Authors' summary.*

21. Pappas, G. (Department of Surgery, Veterans Administration Hospital, 1055 Clermont Street, Denver, Colorado 80220), and J. Burquist. 1970. Creation of dissecting thoracic aortic aneurysms in dogs. J. Surg. Res. 10:333-336.

A technique of creating dissecting thoracic aneurysms in dogs is described. Carbon dioxide under pressure was used to initiate the dissecting process, and an intimal tear was then surgically created. The mortality rate of dissections involving the ascending portion and the arch of the aorta or the entire thoracic aorta was exceedingly high. Dissections involving the descending aorta alone had a more favorable outlook. This experimental model may prove useful in the evaluation of the nature of the lesions and efficacy of various forms of treatment of this disease entity. - *Authors' summary.*

22. Wilkins, R. H. (Division of Neurosurgery, Durham Veterans Administration Hospital, Durham, North Carolina), and P. Levitt. 1970. Intracranial arterial spasm in the dog. A chronic experimental model J. Neurosurg. 33:260-269.

A chronic canine model for the investigation of intracranial arterial spasm was designed and used to study spasm produced by rapid and slow cisternal injections of fresh or heparinized autogenous whole blood, or serum from incubated autogenous blood. Spasm so produced begins within 10 minutes after the injection and lasts from several hours to days. It affects primarily the major arteries of the circle of Willis, especially the proximal anterior cerebral arteries, and it does not seem to involve the extradural arterial tree. In many respects, the intracranial arterial spasm in the present canine model resembles its human counterpart. - *Authors' abstract modified.*

23. Younger, R. K. (S. R. Light Laboratory for Surgical Research, Department of Surgery, Vanderbilt University Medical Center, Nashville, Tennessee), H. W. Scott, Jr., W. H. Butts, and S. E. Stephenson, Jr. 1969. Rapid production of experimental hypercholesterolemia and atherosclerosis in the rhesus monkey: Comparison of five dietary regimens. J. Surg. Res. 9:263-270.

In an effort to develop a stable and reproducible model for surgical research purposes, five dietary regimens designed to produce hypercholesterolemia and atherosclerosis in rhesus monkeys are compared. The combination of ¹³¹I-induced hypothyroidism with a 5% or 10% cholesterol diet has produced the most satisfactory experimental model. - *Authors' summary.*

24. Vakilzadeh, J. (Department of Community Health Sciences, VM-Box 3180, Duke University Medical Center, Durham, North Carolina 27706), D.T. Rowlands, Jr., B. F. Sherwood, and J. C. LeMay. 1970. Experimental bacterial endocarditis in the opossum (*Didelphis virginiana*). II. Induction of endocarditis with a single injection of *Streptococcus viridans*. J. Infect. Dis. 122:89-92.

The high rate of occurrence of spontaneous bacterial endocarditis in adult opossums (*Didelphis virginiana*) and its elimination under appropriate laboratory conditions suggested that this animal might be an excellent model for the study of experimental endocarditis. This paper reports the induction of bacterial endocarditis in opossums by a single injection of *Streptococcus viridans*. - *Authors' abstract.*

EAR

25. Rankin, J. D. (Division of Otolaryngology, University of Vermont Medical School, Burlington, Vermont 65401), and C. S. Karmody. 1970. Serous otitis media. An experimental model. Arch. Otolaryng. 92:14-23.

In the squirrel monkey noninflammatory mechanical obstruction of the eustachian tube results in the collection of a clear straw-colored, nonpurulent fluid in the tympanum. At the present time it is presumed that the fluid collection is the direct result of mechanical obstruction of the tube, although this was demonstrated histologically in only 2 out of 13 animals. The alternative possibility is lymphatic obstruction. It is significant that 93% of the animals developed a clear fluid which has the characteristics of a transudate. In clinical medicine one finds different types of middle ear effusions, all of which are labeled generically as serous otitis media. As it has been possible in this experiment to produce, with a simple technique, the same type of non-inflammatory fluid in 93% of our animals, it is believed that this represents the creation of a reliable experimental model which can be used for further investigations into the etiology of the other generic forms of serous otitis media. - *Authors' abstract.*

ENDOCRINE SYSTEM

26. Brown, G. M. (Ontario Mental Health Foundation Research Scholar; Head, Neuroendocrinology Research Section, Clarke Institute of Psychiatry, Toronto 130, Ontario, Canada), L. J. Gota, D. P. Penny, and S. Reichlin. 1970. Adrenal regulation in the wild captive squirrel monkey: A model of chronic stress. Canad. Psychiat. Assn. J. 15:425-431.

Wild captive squirrel monkeys have unusually high resting cortisol levels and are capable of responding to stress with a tripling of cortisol. The high levels are relatively resistant to dexamethasone blockade. These findings suggest that there is a high hypothalamic set point for cortisol feedback in this species and that the adrenal stress response is difficult to suppress. The authors point out that adrenal regulation in the squirrel monkey represents an unusual adaptation to the environment, which is similar to the increased adrenal activity seen in man during pathological emotional states. - *Authors' summary modified.*

27. Iwatsuka, H. (Biological Research Laboratories, Research and Development Division, Takeda Chemical Industries, Ltd., Osaka, Japan), A. Shino and A. Suzuoki. 1970. General survey of diabetic features of yellow KK mice. Endocrinol. Japon. 17:23-25.

Yellow KK mice, carrying the yellow obese gene (*A⁻*), developed marked adiposity and diabetic symptoms in comparison with their control littermates, black KK mice. The blood glucose and circulating insulin levels were increased progressively from 5 weeks of age in yellow KK mice. Age dependent alterations were also

observed in pancreas and kidney. Namely, degranulation and glycogen infiltration of B cells, first observed at 5 weeks of age, were followed by hypertrophy and central cavitation of islets. Renal glomerular changes, which were very similar to diffuse or exudative type of sclerosis in human diabetes, were also recognized in the mice at 16 weeks of age. These changes, though less remarkable, were also noted in their control littermates older than 16 weeks of age. Some metabolic defects were developed, as demonstrated by in vitro experiments. At younger age, lipogenesis by liver and adipose tissue was increased in yellow KK mice, but there was no noticeable difference in glucose oxidation by adipose tissue between both mice. Insulin sensitivity of adipose tissue was decreased with age in both mice, especially in yellow KK mice being reduced more remarkably to its complete loss at 16 weeks of age. These findings indicate that the yellow obese gene not only induces adiposity but also accelerates development of diabetic traits of KK mice. A possible mechanism for the observed diabetogenic action of the gene will be discussed. -Authors' synopsis.

28. Packer, J. T. (Department of Pathology, University of Missouri Medical Center, Columbia, Missouri 65201), S. D. Rose, R. A. Stuhlman, and L. R. Nelson. 1970. Diabetes mellitus in *Mystromys albicaudatus*. Arch. Pathol. 89:410-415.

Spontaneous diabetes mellitus has developed in a colony of South African hamsters or white-tailed rats, *Mystromys albicaudatus*. Diabetes in this species is characterized by hyperglycemia, polyuria, glycosuria, ketonuria, and severe degenerative changes in the pancreatic islets of Langerhans. Obesity is not associated with hyperglycemia in *Mystromys*. No relationship to laboratory dietary influence has been detected. Hyperglycemia is well established in many animals by the age of 4 months and appears to shorten the life expectancy of this normally long-lived rodent. A strong predilection for the disease in males suggests that in this species the disorder may be sex-linked. - Authors' abstract.

29. Yokote, M. (Freshwater Fisheries Research Laboratory, Tokyo, Japan). 1970. Sekoke disease, spontaneous diabetes in carp, *Cyprinus carpio*, found in fish farms. I. Pathological study. Bull. Freshwater Fish. Res. Lab. 20:39-72.

A histopathological study was carried out on 250 Sekoke carp with diabetic syndrome and 100 normal carp as controls. As the results of the study, very characteristic findings were recognized in the diseased carp. Histological changes in the pancreatic islet tissues of the diseased carp examined were characterized by degranulation of the B cells, decrease in number of the B cells, glycogen infiltration of the B cells, and proliferation of the clear cells of uncertain identity. Glomerular lesions, comprising diffuse intercapillary glomerulosclerosis, hyaline thickening of Bowman's capsular epithelium and the basement membrane, and capsular drop, were characteristically observed in the kidney of the diseased carp. These alterations are closely similar and seem to be counterparts of lesions described in diabetes mellitus in man and other animals. Retinal lesions observed in the carp also resembled those in diabetic retinopathy in man and other animals. From these and other findings presented, it is concluded that the histopathology of Sekoke disease closely resembles that of diabetes mellitus in man. - M.J.A.

EYE

30. Aronson, S. B. (Eye Research Laboratories, Department of Ophthalmology, San Francisco General Hospital, University of California School of Medicine, San Francisco, California), and R. Sasseti. 1970. Experimental ocular hypersensitivity to polypepinephrine and its analogues. Invest. Ophthal. 9:12-19.

Experimental hypersensitivity to epinephrine and to some of its analogues was induced in the rabbit. These changes included chemosis, limbal hyperemia, subepithelial corneal infiltrates, and anterior chamber cells and flare; changes already described in human epinephrine hypersensitivity. Positive skin reactions and circulating antibody were recorded after systemic immunization to polypepinephrine; only skin sensitivity occurred in polyaldomet immunization. This experimental model closely simulates epinephrine hypersensitivity as seen in man. - *Authors' abstract.*

31. Gerke, J. R. (College of Optometry, Pacific University, Forest Grove, Oregon 97116), and M. V. Magliocco. 1971. Experimental Pseudomonas aeruginosa infection of the mouse cornea. Infect. Immun. 3:209-216.

Pseudomonas aeruginosa infection of human cornea is rare but serious. The work of previous investigators using experimental infection primarily of rabbit cornea resulted in successful therapy for 10 to 50% of clinical cases. In this study, the advantage of using the mouse is demonstrated. The methods adapted for characterizing the untreated experimental infection included: incising the cornea to enable establishing the infection; corneal examination with stereoscopic microscope; grading corneal pathology; qualitative and quantitative monitoring of the infecting bacteria by culturing and staining sectioned and dissected tissues. The characteristics of the tissue pathology, host response, and infection were similar to those reported for other animals and man. Corneal pathology was frequently nearly maximal 1 day after infection; host response involved a progression of events of long duration; pathology persisted well beyond the period of bacterial infection. The infection was essentially noncommunicable, and invasiveness was limited to the tissues of the incised eye. The results show the possibility of tests for invasiveness of clinical isolates and for screening for therapeutic and prophylactic measures. Thus, this report describes the experimental infection in the mouse and demonstrates its utility as a model of human disease. - *Authors' abstract modified.*

32. Krohn, D. L. (Institute for Medical Research and Studies, 220 E. 23rd Street, New York, New York 10010), R. Brandt, A. Morris, and A. S. Weston. 1970. Subchoroidal transplantation of experimental malignant melanoma. Amer. J. Ophthal. 70:753-756.

An experimental amelanotic malignant melanoma has been successfully grown in the subchoroidal space of young white New Zealand rabbits. Growth occurred in 20 of 22 attempted transplantations. The tumor in this location, when large enough to be clearly identified ophthalmoscopically but still in an early

growth phase, affords a previously unavailable, convenient model for studies of identification and treatment techniques. Thus, this experimental model may be useful in studies ultimately leading to improved management of clinically encountered intraocular tumors. - *Authors' summary modified.*

HEMATOPOIETIC SYSTEM

33. Argano, S. A. P. (Department of Medicine, Section of Hematology, The Brookdale Hospital Center, Brooklyn, New York), M. S. Tobin, and D. M. Spain. 1969. Experimental induction of myelofibrosis with myeloid metaplasia. Blood 33:851-858.

A simple and reproducible model for inducing a form of myelofibrosis with myeloid metaplasia by the injection of saponin intravenously is described. The histologic lesions produced in rabbits resembled those of agnogenic MMM in man. - *Authors' summary modified.*

34. Dodds, W. J. (Division of Laboratories and Research, New York State Department of Health, Albany, New York 12201). 1970. Canine von Willebrand's disease. J. Lab. Clin. Med. 76:713-721.

Von Willebrand's disease was detected in a family of German shepherd dogs. The defect is characterized by prolonged bleeding time, low factor VIII level, reduced platelet adhesiveness, and abnormal prothrombin consumption. The propositus and 2 other members of the family were severely affected and bled to death. Seven mildly affected members were detected by laboratory tests and may have a heterozygous form of the disease. Infusions of normal or hemophilia A plasma into these "heterozygotes" corrected their platelet adhesiveness defect and produced the paradoxical increase of factor VIII activity seen in human and porcine von Willebrand's disease. Canine von Willebrand's disease appears to provide a suitable model for study of this phenomenon. - *Author's abstract.*

35. Feinstein, R. N. (Division of Biological and Medical Research, Argonne National Laboratory, Argonne, Illinois). 1970. Acatlasemia in the mouse and other species. Biochem. Genet. 4:135-155.

Genetic control of the level of blood catalase activity was first demonstrated in 1927. At present, such control has been demonstrated or suggested for 9 different species, including man, the most studied. The development of an acatalasemic strain of mice has permitted a wide variety of experimental approaches, including most of those used in humans. Among those approaches which cannot readily be applied to man but have been used in acatalasemic mice are investigations of sensitivity to radiation lethality, mechanism of awareness to radiation, possible use as a model for replacement therapy for inborn errors of metabolism, and catalase in tissues other than erythrocytes. These are described, together with genetic, immunological, and other studies comparable to similar work on acatalasemic humans. - *Author's abstract.*

36. Fikrig, S. M. (Department of Pediatrics, State University of New York, Downstate Medical Center, Brooklyn, New York), and S. Berkovich. 1969. Virus induced aplastic crisis in mice. Blood 33:582-589.

Following infection with Coxsackie B₄ virus, 2 inbred strains of mice, NZB/B1 with autoimmune hemolytic anemia and CBA/T6 without hematologic disorder, developed changes in peripheral blood and in bone marrow similar to those described in aplastic crisis in man. A marked decrease or complete disappearance of reticulocytes from the peripheral blood was associated with a decrease in the total number of red cell precursors in the bone marrow. Both findings were temporary; recovery was spontaneous. The hematologic findings were independent of both age and sex in the CBA/T6 animals. By contrast, in the NZB/B1 strain only females between the ages of 4-8 months developed hematologic abnormalities. The etiologic relationship that has been established between Coxsackie B₄ virus infection and aplastic crisis in the test mice suggests that viral agents may play an etiologic role in the pathogenesis of aplastic crisis in man. - *Authors' summary.*

37. Fox, R. R. (The Jackson Laboratory, Bar Harbor, Maine 04609), H. Meier, D. D. Crary, D. D. Myers, R. F. Norberg, and C. W. Laird. 1970. Lymphosarcoma in the rabbit: Genetics and pathology. J. Nat. Cancer Inst. 45:719-729.

Lymphosarcoma occurred often in the WH strain of rabbits and had a hereditary basis. Lymphosarcoma appeared in 16 females and 13 males. The inheritance indicated an autosomal recessive gene conferring susceptibility to lymphosarcoma. We designated this gene ls. Our data were compatible with both concepts of genetic susceptibility to lymphosarcoma and vertical transmission of a virus. Affected rabbits usually died between the ages of 5 and 13 months. The neoplastic involvement of lymphoreticular organs and other organs, especially kidneys, corresponded to a pattern observed in lymphosarcoma of other domestic animals. Specifically, it resembled in many ways visceral lymphosarcomatosis of cats which has been proved unequivocally to be caused by feline leukemia virus. This similarity between rabbit and cat lymphosarcomas involved both sites of onset and distribution of the neoplastic lesions and the hematologic findings of a predominantly aleukemic picture. However, in rabbit lymphosarcomas, often a relative increase in lymphoid cells was found which included both immature and atypical forms. Because rabbits are valuable in laboratory investigations, the finding of lymphosarcoma provides a new and important model for oncogenic studies. - *Authors' summary.*

38. Gillman, T. (Department of Experimental Pathology, Agricultural Research Council, Babraham, Cambridge, England), M. Kinns, and R. M. Cross. 1969. Hodgkin's disease: A possible experimental model in rats. Lancet 2:1421-1422.

This report describes research on experimentally induced and transplantable malignant Hodgkin's-like lesions in rats. Utilization of this potentially important experimental model of Hodgkin's disease may shed further light on the basic nature of the disease in humans. It is postulated that the model in the rat may prove useful in studying the histogenesis and cytogenesis of Hodgkin's disease in man; it may also assist in screening therapeutic measures that may be of value in man. The authors conclude that such studies may assist in unravelling the numerous puzzling aspects of the Hodgkin's disease "maze" in man and also of possible related varieties of spontaneous lymphomata common in domestic animals. - *M.J.A.*

39. Lingeman, C. H., and F. M. Garner (eds.). 1969. Comparative morphology of hematopoietic neoplasms. Nat. Cancer Inst. Monogr. 32. U.S. Dept. Health, Education, and Welfare, Public Health Service, National Cancer Inst., Bethesda, Maryland. 365 pp.

This monograph is the proceedings of an international symposium on "Comparative Morphology of Hematopoietic Neoplasms," which was jointly sponsored by the Registry of Comparative Pathology, Armed Forces Institute of Pathology, and the National Cancer Institute. The publication contains extensive information pertaining to the morphology of spontaneous leukemias, lymphomas, and related neoplasms in a wide range of species, from invertebrates to man. - *M.J.A.*

40. Lozzio, B. B. (University of Tennessee Memorial Research Centre and Hospital, Knoxville, Tennessee 37920), T. P. McDonald, R. D. Lange, M. J. Cawein and A. I. Chernoff. 1970. Splenomegaly and haematologic disorders of the Gunn rat. Brit. J. Haematol. 19:543-554.

Although the Gunn rat has been used extensively as an experimental model for studies of bilirubin metabolism, functions other than those related to the defect of bilirubin conjugation have not yet been examined. This paper reports the presence of naturally occurring splenomegaly and an associated haematologic disorder in homozygous female Gunn rats. Erythrocyte values, leucocyte counts, haemoglobin components and erythropoietin levels were determined in Wistar and Gunn rats. Spleen and bone marrow examinations were also performed. Erythrocyte values and leucocyte counts in Gunn rats were lower than in Wistar rats. Females of both strains of rats showed lower haematocrit values, haemoglobin concentrations, erythrocyte counts, and erythropoietin levels than did the males. Female Gunn rats also had leucopenia when compared with the males. The leucopenia disappeared after castration. The erythrocyte abnormalities were particularly marked in homozygous female Gunn rats which manifested anaemia, shortened erythrocyte survival time and splenomegaly. After splenectomy and/or ovariectomy, the erythrocyte survival time became normal and the anaemia improved. However, ovariectomy alone did not influence the splenomegaly nor the enhanced splenic sequestration of erythrocytes. Microscopic examination of the bone marrow of Gunn rats revealed normal overall cellularity. In contrast, hyperplasia of the white and red pulp was observed in the spleens of Gunn rats of both sexes. These findings suggest that the anaemia of homozygous female Gunn rats is caused by enhanced sequestration of erythrocytes in the spleen and by a possible disturbance of oestrogen metabolism. - *Authors' summary modified.*

41. McKay, D. G. (Department of Pathology, University of California School of Medicine, San Francisco General Hospital, San Francisco, California 94110), A. N. Whitaker and V. Cruse. 1969. Studies of catecholamine shock. II. An experimental model of microangiopathic hemolysis. Amer. J. Pathol. 56:177-200.

Continuous intravenous infusion of epinephrine in high doses into monkeys and rabbits caused shock and disseminated intravascular coagulation and hemolysis. In essence, the hemolysis was characterized by an elevation of plasma hemoglobin, an increase in osmotic fragility, and changes in the shapes of red blood cells. Hemolysis produced by epinephrine infusion resembles that which occurs in the microangiopathic hemolytic anemia syndrome and is ultimately due to (1) disseminated intravascular coagulation, (2) distortion and fragmentation of red cells in their passage through gaps in the capillary endothelium, and (3) acquired spherocytosis. - *Authors' summary modified.*

42. Morley, A. (Department of Medicine and Research, St. Elizabeth's Hospital, 736 Cambridge Street, Brighton, Massachusetts 02135), and F. Stohlman, Jr. 1970. Cyclophosphamide-induced cyclical neutropenia. An animal model of a human periodic disease. *New Eng. J. Med.* 282:643-646.

An animal model of a human periodic disease, cyclical neutropenia, was produced in 5 of 9 dogs by administration of a constant daily dose of cyclophosphamide so as to cause mild bone-marrow depression. That this would occur was predicted by a computer model in which granulopoiesis was regarded as being controlled by two feedback loops, one regulating rate of production and the other rate of release of neutrophils. Cyclical neutropenia does not appear to be a specific entity, and its periodicity, and by extension possibly that of other periodic diseases, may be due to the action of feedback control. A hypothetical possibility is that if unrecognized oscillation of blood cell numbers should develop in patients receiving marrow-depressant drugs, estimate of marrow function at any one point of time might give a wrong impression of overall drug effect. - *Authors' abstract.*

43. Topley, E. (National Blood Transfusion Service, South London Transfusion Centre, Sutton, Surrey), L. J. Bruce-Chwatt, and J. Dorrell. 1970. Haematological study of a rodent malaria model. *J. Trop. Med. Hyg.* 73:1-7.

The present preliminary report describes the haematological changes in a rodent malarial model, and suggests its suitability for further investigations of the underlying pathology of malarial anaemia. The 17X strain of P. berghei yoelii maintained by cyclical transmission through mice (Theiler's original strain) and Anopheles stephensi was used to produce parasitaemia and anaemia in an inbred strain of Balb/C mice inoculated from the second blood passage following mosquito transmission. The pattern of spontaneously remitting anaemia produced in this way showed great reproductibility and a similarity to the anaemia of malaria in man which suggests that it would be a valuable model for further haematological studies. - *Authors' summary modified*

44. Voller, A. (Nuffield Institute of Comparative Medicine, Regents Park, London, N.W.1, England), C. M. Hawley, W. H. G. Richards, and D. S. Ridley. 1969. Human malaria (Plasmodium falciparum) in owl monkeys (Aotus trivirgatus). *J. Trop. Med. Hyg.* 72:153-160.

Findings from studies of human malaria strongly suggest that in the disease, platelets and clotting factors become depleted as a result of diffuse intravascular coagulation. The results of this study suggest that a similar condition occurs in owl monkeys infected with Plasmodium falciparum, which closely parallels the situation in humans infected with this same parasite, although so far there is no histological evidence that the condition progresses to the stage of occlusive thrombosis. The similarity of the pattern of the disease in man and Aotus suggests that this animal may be useful for the clinical study of P. falciparum, for which none of the other mammalian malaria model systems are satisfactory. -M.J.A.

MUSCULOSKELETAL SYSTEM

45. Cobb, L. M. (Chester Beatty Research Institute, Institute of Cancer Research, Royal Cancer Hospital, London, S.W.3, England). 1970. Radiation-induced osteosarcoma in the rat as a model for osteosarcoma in man. Brit. J. Cancer 24:294-299.

A technique is described for the local induction of osteosarcoma in the rat by implanting ³²P-impregnated polyvinyl chloride discs into the distal femoral metaphysis. The incidence of osteosarcomata after 18 months was 28%. A comparison is made of the pathology of the radiation-induced osteosarcoma in the rat and the "spontaneous" osteosarcoma in man. The possible value of the rat osteosarcoma model is discussed. - Author's summary.

46. James, C. C. M. (Regional Neurological Center and Department of Pathology, Newcastle General Hospital, Newcastle on the Tyne, England), L. P. Lassman, and B. E. Tomlinson. 1969. Congenital anomalies of the lower spine and and spinal cord in Manx cats. J. Pathol. 97:269-276.

Manx cats may show disabilities resembling those found in some cases of human spina bifida. The clinical and pathological findings in the cats and in human spina bifida are briefly compared. - M.J.A.

47. Klein, F. (Institute of Rheumatism Research, Leiden, The Netherlands), P. Mattern, and H. J. Kornman-v.d. Bosch. 1970. Experimental induction of rheumatoid factor-like substances in animal trypanosomiasis. Clin. Exp. Immunol. 7:851-863.

Rheumatoid factor-like substances were induced in rabbits by infection with Trypanosoma equiperdum. There was a certain parallelism with the phenomena described earlier with T. gambiense infections in man. In the experiments the chemical nature of the rheumatoid factor-like substances and their relation to Ig levels as a function of the infection have been studied in particular. The anti-IgG globulins were IgM with a preference for heterologous (human) IgG in the latex fixation test. A correlation was found between the latex fixation titres and the IgM levels in the sera. A naturally occurring pre-infectious agglutinator was not of IgM nature. The anti-IgG globulins developed in all the

infected animals, mostly within 2 weeks and often before the IgG levels in the sera started to increase. The failure to induce rheumatoid factor-like substances in mice infected with a certain strain of T. gambiense indicates the importance of the host-parasite relationship for the formation of rheumatoid factors. These experiments might form the basis of a model for investigating the nature of rheumatoid factor formation. - *Authors' summary modified.*

48. Miller, M. L. (Department of Internal Medicine, University of Utah College of Medicine, Salt Lake City, Utah), J. R. Ward, B. C. Cole, and E. A. Swinyard. 1970. Six-sulfanilamidoindazole induced arthritis and peri-arthritis in rats. A new model of experimental inflammation. *Arthrit. Rheumat.* 13:222-235.

Several oral or subcutaneous administrations of 6-sulfanilamidoindazole (6-SAI) to adult rats regularly induced acute, self-limiting arthritis and peri-arthritis confined primarily to the hind paws. The incidence of arthritis in orally medicated rats was related, in part, to the body weight of the animals at time of the initial feeding. Histologically, the lesions were nonsuppurative and proliferative. Lymphocytes were present in all stages of inflammation preceding the appearance of fibroblasts which were the most consistent and striking cellular components. Inflammation was not associated with anemia, elevation of serum uric acid and blood urea nitrogen concentrations, or alteration in sedimentation rates and total and differential WBC counts. Evidence is presented which suggests that the phlogistic effects of 6-SAI are independent of crystal formation in the periarticular tissues, provocation of latent mycoplasma infections, kinin formation through activation of the Hageman factor, immediate and delayed type hypersensitivity reactions, and induction of an anaphylactoid-like reaction. - *Authors' abstract.*

49. Norden, C. W. (Department of Medicine, University of Rochester, School of Medicine, 260 Crittenden Boulevard, Rochester, New York 14620). 1970. Experimental osteomyelitis. I. A description of the model. *J. Infect. Dis.* 122:410-418.

This paper reports the establishment of a model of chronic osteomyelitis. It is suggested that this rabbit model, whose pathologic and radiologic appearances are similar to those in the human disease, can be used to explore unanswered questions about the pathogenesis and therapy of osteomyelitis. - *C.B.F.*

50. Murphy, H. M. (M.R.C. Experimental Genetics Unit, Department of Animal Genetics, University College, London, England). 1969. A review of inherited osteopetrosis in the mouse. Man and other mammals also considered. *Clin. Orthopaed. Rel. Res.* 65:97-109.

There is little doubt that the osteopetrosis encountered in the mouse, rat, rabbit, calf and man is the same pathologic condition, although it varies in intensity within species and between species. The mouse disease, which is the more severe type, provides an opportunity for a further study of the developmental defects, bone dynamics and pathogenesis of osteopetrosis, which may lead to a better understanding of the human disorder. - *Authors' summary.*

51. Ritsila, V. A. (Orthopaedic Hospital, Invalid Foundation, Helsinki, Finland). 1969. Talipes equinovarus and vertical talus produced experimentally in newborn rabbits. Acta Orthopaed. Scand. Suppl. 121. 87 pp.

The aim of this study was to produce in young rabbits imitations of the congenital foot deformities encountered in man, by provoking changes in the soft tissues. By means of transections and resections of tendons and muscles, tenodeses, transections of ligaments, and fixation in plaster in extreme positions, it was found possible to produce a number of imitations of foot deformities found in humans; those corresponding to talipes equinovarus and vertical talus are described. Marked talipes equinovarus deformity was produced in 32 rabbits, and vertical talus in 51. The course of development of the deformity was followed during growth by repeated radiography. The deformities produced were analyzed by dissection and photography of the feet of 75 animals killed at different ages. Sections for histological examination were taken from 8 animals. In both a macro- and micro-anatomical and radiological sense, great similarities were observed between the deformities in rabbits and those encountered in humans. - M.J.A.

NERVOUS SYSTEM

52. Ausman, J. I. (Department of Neurosurgery, University of Minnesota Hospitals, Minneapolis, Minnesota 55455), W. R. Shapiro, and D. P. Rall. 1970. Studies on the chemotherapy of experimental brain tumors: Development of an experimental model. Cancer Res. 30:2394-2400.

A method of rapidly implanting tumors intracerebrally in large numbers of mice is described. Four tumors previously induced by carcinogen implantation into brains of mice were used. Histologically and biologically, they were gliomas (ependymoblastoma). The pathology of the tumors, their pathogenesis in the host brain, and the clinical course of tumor-bearing animals was evaluated. The average median day of death and the number of animals surviving longer than 60 days from failure of the tumor to take were determined and are presented. The advantages and disadvantages in the use of these animal systems in intracerebral tumor models are discussed. - *Authors' summary.*

53. Baringer, J. R. (Department of Neurology, Massachusetts General Hospital and Harvard Medical School, Division of Infectious Diseases, Children's Medical Center, Boston, Massachusetts 02115), and J. F. Griffith. 1970. Experimental measles virus encephalitis. A light, phase, fluorescence, and electron microscopic study. Lab. Invest. 23:335-346.

The Edmonston strain of measles virus has been successfully adapted to produce an encephalitis when injected intracerebrally into newborn hamsters. The neuropathologic features of the illness were studied by conventional histologic techniques, by immunofluorescence microscopy, and by phase and electron microscopy. The relationships of this model of measles encephalitis to the conditions occurring in humans after measles virus infection are discussed. - *Authors' abstract modified.*

54. Chamberlain, J. G. (Department of Anatomy, University of California at San Francisco, San Francisco, California 94122). 1970. Early neurovascular abnormalities underlying 6-aminonicotinamide (6-AN)-induced congenital hydrocephalus in rats. *Teratology* 3:377-388.

Defects in the rat central nervous system during retarded brain development and congenital hydrocephalus were studied following single maternal injections of the niacinamide antimetabolite 6-aminonicotinamide (6-N) late in development. Histological and histochemical analyses indicated CNS hemorrhage and growth retardation of fetal brains 24 hours after treatment; fluid movement into cerebral ventricles was evidenced by secretionlike, circular "blebs" along the ependymal lining. There was transiently increased glycogen in hypoplastic choroid plexuses with disruption of cerebral layering of neuroblasts. Despite thinned cerebral cortex and increased ventricular surface area, associated with cranial distortion and communicating, compensatory ventricular enlargement, normal intracranial pressure was recorded by day 21 of gestation. During the pathogenetic process macrophagic cells removed cellular debris and RBC's so that by term little evidence of early hemorrhage was apparent. - *Author's abstract.*

55. Crawford, R. D. (Department of Poultry Science, University of Saskatchewan, Saskatoon, Saskatchewan, Canada). 1970. Epileptiform seizures in domestic fowl. *J. Hered.* 61:185-188.

A new mutant causing epileptiform seizures in the domestic fowl has been described. The condition is controlled by a single autosomal recessive gene having incomplete penetrance. The proposed gene symbol is epi. The gene is independent of 7 autosomal dominant marker genes. The seizures occur throughout the life span of the bird. They appear to be triggered by "nervous fatigue"--as for instance from strong visual or auditory stimuli and from muscular exertion. They bear a certain resemblance to grand mal epilepsy in humans. The seizures do not appear to impair growth rate, livability, or gamete production if the affected birds are provided with a sheltered environment. - *Author's summary.*

56. Eckroade, R. J. (Department of Pathology, University of Wisconsin Medical School, Madison, Wisconsin 53706), G. M. Zu Rhein, R. F. Marsh, and R. P. Hanson. 1970. Transmissible mink encephalopathy: Experimental transmission to the squirrel monkey. *Science* 169:1088-1090.

A progressive, fatal spongiform encephalopathy developed in three squirrel monkeys 11 months after inoculation with primate-passaged transmissible mink encephalopathy agent. The clinical symptoms and histopathologic and electron microscopic findings suggest that this naturally occurring disease of mink has been transmitted experimentally to squirrel monkeys. Transmissible encephalopathy of mink in squirrel monkeys provides a readily available inexpensive primate model for the study of "subacute spongiform viral encephalopathies." This investigation lends support to the suggested relationship between animal and human transmissible viral encephalopathies. - *Authors' abstract modified.*

57. Grimm, R. J. (Laboratory of Neurophysiology, Good Samaritan Hospital and Medical Center, Portland, Oregon 97210), J. G. Frazee, T. Kawaski, and M. Savic. 1970. Cobalt epilepsy in the squirrel monkey. *Electroenceph. Clin. Neurophysiol.* 29:525-528.

Small amounts of cobalt powder will generate paroxysmal activity for 48-72 hours in the unanesthetized squirrel monkey cortex. Using halothane anesthesia with a rapid recovery time, paroxysmal activity may begin within 30 minutes of cobalt application. Discharges can be segregated by wave form, frequency and pattern into four clearly identifiable phases. Illustrations of these phases are given. As good signal-to-noise characteristics of paroxysmal events are obtainable, this model of focal epilepsy in squirrel monkeys is open for quantification techniques. - *Authors' summary.*

58. Harrington, D. D. (Department of Veterinary Science, University of Kentucky, Lexington, Kentucky 40506), and P. M. Newberne. 1970. Correlation of maternal blood levels of vitamin A at conception and the incidence of hydrocephalus in newborn rabbits: An experimental animal model. *Lab. Anim. Care* 20:675-680.

Rabbits born to females which have been maintained on vitamin A-deficient diets for long periods of time prior to breeding may be hydrocephalic at birth. A deficiency state sufficient to result in hydrocephalic offspring did not affect litter size, but hydrocephalic neonates were significantly smaller than controls. Stillborn litters occasionally were produced, but anomalies other than hydrocephalus were rare. One animal was stunted, microcephalic, gastro-schistic, and lacked eyelids. The critical maternal blood levels of vitamin A below which a significant incidence of hydrocephalus was seen were found to be between 20 and 30 ug/100 ml of serum. When maternal blood levels were below 20 ug/100 ml of serum at conception, 70% of the litters were entirely hydrocephalic. Rabbits which had previously produced litters which contained hydrocephalics failed to produce additional litters unless first supplemented with vitamin A. The occurrence of hydrocephalus in subsequent litters was again found to depend upon maternal blood levels of vitamin A at conception and during gestation. - *Authors' summary.*

59. McClure, H. M. (Department of Veterinary Pathology, Yerkes Regional Primate Research Center, Emory University, Atlanta, Georgia 30322), K. H. Belden, W. A. Pieper, and C. B. Jacobson. 1969. Autosomal trisomy in a chimpanzee: Resemblance to Down's syndrome. *Science* 165:1010-1012.

An infant chimpanzee (*Pan troglodytes*) with clinical, behavioral, and cytogenetic features similar to those in Down's syndrome is described. The infant shows retarded growth rate, congenital abnormalities, retarded neurologic and postural development, epicanthus, hyperflexibility of the joints, muscle hypotonia, and trisomy of a small acrocentric chromosome. - *Authors' abstract.*

60. Samorajski, T. (Laboratory of Neurochemistry, Cleveland Psychiatric Institute and Institute of Pathology, Case-Western Reserve University, Cleveland, Ohio 44109), R. L. Friede, and P. A. Reimer. 1970. Hypomyelination in the quaking mouse. A model for the analysis of disturbed myelin formation. J. Neuropathol. Exp. Neurol. 29:507-523.

In the present investigation a quantitative histologic and electron microscopic study of glial cell density and axon-sheath relationship was undertaken on samples of optic nerve, pyramidal tract, and sciatic nerves of control and quaking mice to determine if myelin deficiency involves any additional morphologic components. The data show that the quaking mutant provides an excellent experimental model for the study of a disease characterized by a deficient myelination. The defect can be attributed to an insufficient production of myelin by the sheath cells of both the central and peripheral nervous systems, which results in a condition which we define as a "hypomyelination." This report also includes some preliminary results of an ultrastructural study of myelin formation in nerve tissue obtained from the "Ataxic" mutant mouse. - *Authors' abstract modified.*

61. Sauer, R. M. (National Zoological Park, Washington, D.C. 20009), B. C. Zook, and F. M. Garner. 1970. Demyelinating encephalomyelopathy associated with lead poisoning in nonhuman primates. Science 169:1091-1093.

Lead poisoning was diagnosed in four primates by the finding of toxic amounts of lead in tissues. Abnormalities in the brain and spinal cord were characterized by vascular lesions and demyelination. These findings suggest a new animal model for the study of demyelination and strengthen the supposition that lead may be a factor in some idiopathic demyelinating diseases of animals and man. - *Authors' abstract modified.*

62. Wechsler, W. (Max-Planck-Institut für Hirnforschung, Abteilung für Allgemeine Neurologie, Cologne, Germany), P. Kleihues, S. Matsumoto, K. J. Zülch, S. Ivankovic, R. Preussmann, and H. Druckrey. 1969. Pathology of experimental neurogenic tumors chemically induced during prenatal and postnatal life. Ann. N.Y. Acad. Sci. 159(Art. 2):360-408.

This report presents a general outline of the importance of experimental and comparative neurooncology, with the object of contributing to a better understanding of the possible modes of pathogenesis of naturally occurring neurogenic tumors in man. Two principally different modes for experimental chemical neurooncogenesis have been demonstrated: (1) local implantation of chemical carcinogens (topical carcinogens) in different regions of the nervous system, and (2) systemic extraneural administration of resorptive carcinogens with a high specificity for the nervous tissue. This report is based upon a large experimental series using various N-nitroso compounds and especially ENU as resorptive carcinogens capable of producing in a high incidence a variety of neurogenic tumors in BD rats with either multiple or single applications of the chemical by different routes. The occurrence of tumors at consistently preferred location sites in the central and peripheral nervous systems was striking. According to a preliminary classification of the transplacentally

induced neoplasms, the presence of a great variety of isomorphous and pleomorphous gliomas (oligodendrogliomas, astrocytomas, and mixed gliomas) and malignant ependymomas in the brain and spinal cord was demonstrated. Most of the tumors of the peripheral nervous system were considered to be malignant neurinomas with varying degrees of differentiation. Pathogenetically, the neoplasms appeared to originate from individual cells developing into microtumors and finally into isomorphous and pleomorphous macrotumors, thus demonstrating that anaplasia is one of the essential factors in tumor morphogenesis of this type. The dose-effect and time relationships for the carcinogenic action of N-nitroso compounds, the autoradiographic evaluation of DNA synthesis and of the generation cycle, and some ultrastructural characteristics of the tumors cells were presented. If one compares the naturally occurring neurogenic tumors in man with experimentally produced tumors in rats which have been transplacentally induced with ENU, there seem to be similarities as well as differences regarding incidence, topography, and morphology. The fact that not only multiple but also single doses of N-nitroso urea compounds were capable of inducing neurogenic tumors in the adult rat as well as transplacentally in the fetus points to the question whether brain tumors in man may be similarly induced prenatally or postnatally by contact with an as yet unknown extrinsic neuroocogenic agent. The answer to this question, however, is as yet unknown. - *Authors' summary.*

REPRODUCTIVE SYSTEM

63. Andrada, J. A. (The Center for Immunology and Department of Microbiology, School of Medicine, State University of New York at Buffalo, Buffalo, New York 14214), E. C. Andrada, and E. Witebsky. 1969. Experimental autoallergic orchitis in rhesus monkeys. Proc. Soc. Exp. Biol. Med. 130:1106-1113.

Rhesus monkeys were injected with monkey testicular extract incorporated into Freund adjuvant. All six monkeys developed a histological picture of orchitis. The testicular lesions consisted of congestion and serous edema, with sloughing of germinal cells from the tubules; these cells appeared to fill the epididymis ducts. Lesions were more pronounced between 10 and 13 weeks after immunization. Lymphocytic infiltration was present in moderate intensity in only one animal. Circulating antibodies were detected in a few animals at very low titer; however, following castration the titers increased. The organ specificity of the antibody response could be well documented by means of immunofluorescence. According to the results obtained, auto- as well as isosensitization of rhesus monkeys with monkey testicular material incorporated into complete Freund adjuvant produces histological and serological changes very similar to those seen in human experimental orchitis. - *Authors' summary.*

64. Bruere, A. N. (Department of Veterinary Clinical Science, Massey University, Palmerston North, New Zealand), R. B. Marshall, and D. P. J. Ward. 1969. Testicular hypoplasia and XXY sex chromosome complement in two rams: The ovine counterpart of Klinefelter's syndrome in man. J. Reprod. Fertil. 19:103-108.

Two sheep of different breed displayed gross testicular hypoplasia, azoospermia, and apparent aspermatogenesis. The modal chromosome number was 55 in all tissues studied, the extra chromosome being identified as an X from sex chromatin studies on one animal. The abnormalities resemble those of chromatin-positive Klinefelter's syndrome in man, with a comparable incidence and a possibly identical cause in the two species. - *Authors' summary.*

65. Klionsky, B. (Neonatal Department, Hammersmith Hospital, Du Cane Road, London, W.12, England), and J. S. Wigglesworth. 1970. Production of experimental models of foetal growth retardation by inhibition of DNA or protein synthesis. Brit. J. Exp. Pathol. 51:361-371.

Foetal growth retardation was induced in the rat by administration of hydroxyurea, an inhibitor of DNA synthesis, or cycloheximide, an inhibitor of protein synthesis. Each drug was given at 2 stages of pregnancy, either at 15 or at 18 days. Body and organ weights were studied at term (21 days) and DNA, RNA and protein estimations performed on brain and liver, with additional measurements of carbohydrate in the liver. Inhibition of DNA synthesis (hydroxyurea) caused reduction in organ cell population whether given early or late in pregnancy but the effect on the brain was more marked in early pregnancy. Haemopoietic cells in the liver were destroyed by repeated dosage on day 18. Inhibition of protein synthesis (cycloheximide) caused reduction in mean cell weight, but little reduction in cell population whether given early or late. With both drugs the effects on cell population were more severe with administration early in pregnancy. The results indicate that timing, mode of action and severity of stimulus are all important in determining the effect of any particular stress on foetal growth. The implications for studies on human intra-uterine growth retardation are discussed. - *Authors' summary.*

66. McGowan, L. (Department of Obstetrics and Gynecology, The George Washington University Medical Center, Washington, D. C.) and R. H. Davis. 1970. Peritoneal fluid cytology in ovarian tumors of mice. Obstet. Gynecol. 35:878-890.

A procedure for the early detection of developing primary ovarian neoplasms is needed before a substantial decrease in the number of deaths due to ovarian cancer can be attained. Our prior work indicated that the female mouse was the laboratory model most comparable to the woman, from the standpoint of peritoneal fluid cellular composition which was similarly affected in mice and women by estrogen, the hormones of pregnancy, inflammation, and acute radiation. For 1 year we studied the peritoneal fluid cellular distribution and morphology of peritoneal fluid cells in mice of the C3B6F1 W-series, genotype W^X/W^V , all of which developed spontaneous complex tubular adenomas by 7 months of age. The similarity between the histogenesis of this mouse ovarian tumor and the most common ovarian tumors in women was recorded. We could detect the development of primary ovarian neoplasms by a significant change in the cytodifferential cellular patterns of peritoneal fluid. These observations occurred months before morphologic cellular variations appeared in peritoneal fluid, and their value as a possible diagnostic aid for primary ovarian neoplasms in women is stressed. - *Authors' abstract.*

67. Shackleton, C. H. L. (Northwick Park Clinical Centre, Harrow, England), and F. L. Mitchell. 1970. Steroids in primates: Excretion of 3 β -hydroxy- Δ^5 steroids by a newborn chimpanzee (Pan troglodytes). FEBS Let. 11:129-131.

The results of this investigation suggest that the formation of steroids by the newborn chimpanzee is similar to that of the human and that this species may be used as a model for the study of steroid biosynthesis and metabolism by the human newborn and foeto-placenta unit. - *Authors' summary modified.*

68. Wade, M. E. (Department of Obstetrics and Gynecology, Yale University School of Medicine, New Haven, Connecticut 06510), R. O. Gordon, and M. S. Mitchell. 1970. Chemical suppression of primary and anamnestic maternal immunization in Rh-incompatible pregnancies. An animal model. Amer. J. Obstet. Gynecol. 106:286-291.

An animal model demonstrating the use of chemical agents (cytosine arabinoside, cyclophosphamide) as a means of immunosuppression of the primary and anamnestic Rh-immune response is presented. Suppression of this anamnestic response, if applicable in the human Rh system, might be beneficial to the already mildly to moderately sensitized Rh patient by preventing further sensitization. Methods for producing a state of immunologic tolerance in this system are discussed using the Sprague Dawley rat as the animal model. - *Authors' abstract modified.*

RESPIRATORY SYSTEM

69. Corrin, B. (St. Thomas's Hospital Medical School, London, England), and E. King. 1970. Pathogenesis of experimental pulmonary alveolar proteinosis. Thorax 25:230-236.

Rats exposed to various airborne dusts developed a condition identical to pulmonary alveolar proteinosis as seen in man. The experimental condition developed through a stage of endogenous lipid pneumonia, characterized by numerous large foam macrophages widely distributed throughout the lung. These cells broke down to release a finely granular material which finally condensed to reproduce the appearances of alveolar proteinosis. Electron microscopy indicated that the alveolar material was produced by type II pneumocytes and may therefore represent pulmonary surfactant. A study of the dust-handling mechanism showed that in affected animals macrophage mobility was seriously impaired. - *Authors' abstract.*

70. Fink, J. N. (Allergy Section, Department of Medicine, Marquette School of Medicine, Milwaukee, Wisconsin), G. T. Hensley, and J. J. Barboriak. 1970. An animal model of a hypersensitivity pneumonitis. J. Allerg. 46:156-161.

This study was designed to produce a model of a hypersensitivity pneumonitis, pigeon breeders' disease, in experimental animals. Rats were exposed for varying times by inhalation either to pigeon dropping extract, a solution of bovine serum albumin, or a solution of bovine serum albumin containing endotoxin. The animals given pigeon dropping extract developed characteristic histologic and immunologic features of the disease as found in man. No significant pulmonary lesions were found in the control animals. - *Authors' abstract.*

71. Goldring, I. P. (Department of Surgery, Albert Einstein College of Medicine, Yeshiva University, Bronx, New York), S. S. Park, C. S. Shim, L. Greenburg, and I. M. Ratner. 1970. Histopathology and mechanical properties of the lung in experimental emphysema. *Pathol. Microbiol.* 35:176-180.

In this study, an experimental model was utilized to investigate the pathogenesis of the coexistence of chronic bronchitis and pulmonary emphysema in humans. Syrian hamsters were rendered emphysematous by exposure to a papain aerosol, and an attempt was made to induce bronchitis in the animals and to study the effect of this on the severity of the emphysema. It was noted that exposure of the hamsters to an aerosol of papain produced a panlobular emphysema. The effects of age, sex, and exposure to high concentrations of SO₂ on the pathologic appearance and mechanical properties of the lungs were reported. The authors conclude that more widespread use of an experimental model may permit the solution of many of the mysteries of emphysema: its pathogenesis, its relationship to chronic obstructive bronchopathy, the assessment of its extent by physiologic measurements, and even its response to therapy. - *M.J.A.*

72. James, D. E., R. L. Fisk (Surgical-Medical Research Institute, The University of Alberta, Edmonton, Alberta, Canada), C. Gort, and C. M. Couves. 1970. An experimental model for evaluating support systems in acute respiratory distress. *Ann. Thorac. Surg.* 9:36-43.

Acute respiratory distress was produced in dogs by airway restriction. Duration of survival following the time when the rising arterial pCO₂ and the falling pO₂ crossed was very predictable. When the benefits of bypass oxygenation are assessed experimentally by beginning perfusion at the onset of respiratory distress, the anticipated benefits of a similar measure for patients already in distress probably will be overrated. Experimental evaluation of methods for supporting patients in acute respiratory distress should be carried out in a model that simulates clinical respiratory distress. The time during progressive respiratory distress when arterial blood-gas crossing is observed represents an improved model for the study of cardiorespiratory support measures in acute respiratory distress. - *Authors' summary.*

73. Park, S. S. (Albert Einstein School of Medicine, Bronx, New York), I. P. Goldring, I. M. Ratner, C. S. Shim, and L. Greenburg. 1970. Histopathology and mechanical properties of the lung in experimental emphysema. In: A summary of the twelfth Aspen research conference on emphysema and related diseases. *Amer. Rev. Resp. Dis.* 101:445.

An experimental model was developed for the production of emphysema in Syrian hamsters. This method required only a single exposure of animals to an aerosol of papain solution. Because of the ease in controlling the dose of papain administration and the uniformity in the production of emphysema, this method provides a potential tool for exploring various pathogenetic aspects of pulmonary emphysema. Effect of age, sex, and cochallenge with sulfur dioxide on the development of emphysema was studied by comparing the histopathologic and mechanical properties of the lung obtained from treated animals with those of control animals. In animals exposed to an aerosol of papain, a massive, hemorrhagic, inflammatory reaction developed followed by pulmonary emphysema, which progressed to an advanced state within 3 to 6 weeks after treatment and persisted throughout the life span of the animals (up to 16 months of follow-up). The emphysema appeared similar to the panlobular type in humans. - *Authors' summary modified.*

74. Pushpakom, R., J. C. Hogg, A. J. Woolcock, A. E. Angus, P. T. Macklem (Respiratory Division, McGill University Clinic, Royal Victoria Hospital, Montreal, 112 Canada), and W. M. Thurlbeck. 1970. Experimental papain-induced emphysema in dogs. Amer. Rev. Resp. Dis. 102:778-789.

Papain was injected intratracheally into 8 dogs after measurements had been made of oxygen tension, carbon dioxide tension and pH of arterial blood, subdivisions of lung volume, steady state diffusing capacity for carbon monoxide, fractional uptake of carbon monoxide, static pressure-volume curves, and pulmonary resistance at different lung volumes, and measurements were repeated 1 to 4 weeks later. There were no significant changes in arterial blood gas tensions, acid-base balance, or pulmonary resistance, but the diffusing capacity decreased. Total lung capacity, functional residual capacity, and residual volume increased; elastic recoil decreased. Pulmonary resistance was partitioned when the dog was sacrificed; the resistance of airways smaller than 2 mm in diameter was increased whereas that of larger airways was decreased. Trivial to moderate panlobular emphysema was found in all animals on pathologic examination. Internal surface area was reduced, particularly, when it was assessed at a standard lung volume. The mean linear intercept was increased. The disease induced by papain administered intratracheally to dogs was similar both pathophysiologically and morphologically to human panlobular emphysema. - *Authors' summary.*

75. Reid, L. (Department of Experimental Pathology, Brompton Institute and Brompton Hospital, London SW 3, England). 1970. Evaluation of model systems for study of airway epithelium, cilia, and mucus. Arch. Intern. Med. 126:428-434.

An animal "model" of human lung disease provides a means of testing the effect of irritants and of study in pathogenesis. To relate the model to human lung disease it is necessary to establish the morbid anatomy of the disease. The airway lining system which is under scrutiny here is a mucus-secreting surface appropriate for the study of chronic bronchitis, the main features of which in man are hypertrophy of mucus-secreting cells, increase in number of goblet cells and extension to the periphery, and an increase in cell activity. The mitotic count is raised and the type of acid glycoprotein modified. These

changes can be quantified. They can be reproduced in the experimental animal. The rat is chiefly dealt with in this report, as it has been studied in most detail. - *Author's abstract modified.*

76. Strauss, B. (Department of Medicine, College of Physicians & Surgeons, Columbia University, New York, New York 10032), P. R. B. Caldwell, and H. W. Fritts, Jr. 1970. Observations on a model of proliferative lung disease. I. Transpulmonary arteriovenous differences of lactate, pyruvate, and glucose. J. Clin. Invest. 49:1305-1315.

Intravenous injections of complete Freund's adjuvant, used by others to stimulate the reticuloendothelial system of small laboratory animals, produced granulomas resembling sarcoid in the lung of the dog. At the height of the disease, when granulomas occupied more than half of the alveolar tissues, transpulmonary arteriovenous (A-V) differences of lactate, pyruvate, and glucose were measured. When the diseased dogs breathed the room air, the A-V differences of lactate and pyruvate were greater than normal; and when the dogs breathed an hypoxic mixture, the differences increased further. Hence the model affords the opportunity for studying the in vivo metabolism of diseased lungs. It may also prove useful for studying other aspects of granulomatous disease which cannot be easily approached in man. - *Authors' abstract.*

77. Tyrrell, D. A. J. (Clinical Research Centre Laboratories, National Institute for Medical Research, London, N.W.7, England), and C. R. Coid. 1970. Sendai virus infection of rats as a convenient model of acute respiratory infection. Vet. Rec. 86:164-165.

Sendai virus (para-influenza 1) originally recovered from mice was administered to weanling rats intranasally by dropping virus suspension on to the external nares or by exposure to a spray of virus in a closed cabinet. Within 1 week the animals showed signs of respiratory disease from which they usually recovered. In addition, staring coat, diminished activity and loss of weight were evident. Extensive lung lesions were also observed at the height of the disease. Other rats in the same cage acquired the infection, but did not develop obvious signs of illness. It is suggested that (I) the lung disease, previously investigated in a colony of laboratory rats which had antibody to Sendai virus, may have been associated with this agent. (II) The rat may be a useful animal in attempts, for example, to study the effect of respiratory virus infection on nutritional or other problems where a model system is required. - *Authors' summary.*

78. Wardell, J. R., Jr. (Smith Kline & French Laboratories, Philadelphia, Pennsylvania 19101), L. W. Chakrin, and B. J. Payne. 1970. The canine tracheal pouch. A model for use in respiratory mucus research. Amer. Rev. Resp. Dis. 101:741-754.

Although alterations in tracheobronchial secretions are directly implicated in the development of chronic obstructive lung disease, fundamental research on the biosynthesis and secretion of respiratory tract mucus under varying experimental conditions has been hampered by the lack of a suitable animal model. A canine model is described in which a 5-cm to 6-cm segment of the cervical

trachea is separated and formed in situ into a subcutaneously buried pouch. The pouch has been shown to be an independent, histologically normal, physiologically functional, autonomically innervated portion of the corresponding intact airway, suitable for long-term studies on respiratory mucus. The model allows repeated collection of milliliter quantities of respiratory tract mucus, free of demonstrable microorganisms and containing only minimal numbers of cells, under essentially physiologic conditions. The application of the model to studies on the physiologic control of the biosynthesis and secretion of mucus and the role of various possible etiologic factors in the pathogenesis of mucus hypersecretion are discussed. - *Authors' summary.*

SKIN

79. Dajani, A. S., and L. W. Wannamaker (Department of Pediatrics, University of Minnesota, School of Medical Sciences, Box 296, Mayo Memorial Building, Minneapolis, Minnesota 55455). 1970. Experimental infection of the skin in the hamster simulating human impetigo. I. Natural history of the infection. *J. Infect. Dis.* 122:196-204.

Although the clinical, epidemiological, and histopathological aspects of impetigo have been explored, little is known about the pathophysiology of the infection or about the role of bacterial interaction in the lesions of the skin. An experimental model is therefore desirable to explore some of the parameters of this disease, particularly since such answers cannot be easily obtained from study of the human infection. This report describes the use of the Syrian hamster as experimental model, with particular reference to the quantitative aspects and the natural history of the infection. - *M.J.A.*

80. Forrest, I. S. (Biochemical Research Laboratory, Veterans' Administration Hospital, Palo Alto, California), J. C. Kosek, R. C. Aber, and M. T. Serra. 1970. Rabbit as a model for chlorpromazine-induced hyperpigmentation of the skin. *Biochem. Pharmacol.* 19:849-852.

Hyperpigmentation of exposed skin areas, comparable to that seen in less than 1% of patients chronically dosed with chlorpromazine after intensive long-term therapy, has been produced in 16 out of 16 chronically dosed pigmented rabbits, receiving between 20-20 mg/kg per day. Thirty-minutes u.v. irradiation of a clipped or shaved area produced clear-cut hyperpigmentation of naturally pigmented skin areas in about 4 weeks. The characteristic occurrence of granular pigment in the dermis which is normally free of pigment was also observed. Hyperpigmented rabbits did not develop any concomitant ocular pathology, as seen in some patients on long-term, high-dosage chlorpromazine therapy. - *Authors' abstract.*

81. Melish, M. E. and L. A. Glasgow (Department of Pediatrics, University of Rochester, School of Medicine and Dentistry, Rochester, New York). 1970. The staphylococcal scalded-skin syndrome. Development of an experimental model. *New Eng. J. Med.* 282:1114-1119.

A syndrome of dermatologic response to infection with phage Group 2 coagulase-positive staphylococci with reactions ranging from bullous impetigo to generalized

scarlatiniform rash without exfoliation to generalized exfoliative disease was observed in 17 children. Staphylococci isolated from these patients, as well as 2 additional Group 2 organisms, produced exfoliation in newborn mice. The experimental lesion progressed from the development of a Nikolsky sign to bullous formation and then widespread exfoliation. Histologic sections were characterized by a cleavage plane within the epidermis at the stratum granulosum. Among 36 strains, the capacity to produce exfoliation was unique to staphylococci of phage Group 2. The disease produced in newborn mice reproduces the scalded-skin syndrome. Staphylococci may be recovered from involved animals. Thus Koch's postulates are fulfilled, and staphylococci of phage Group 2 are established as the etiologic agent of this syndrome. - *Authors' abstract.*

URINARY SYSTEM

82. Barabas, A. Z. (Department of Pathology, Queens University of Belfast, Belfast, Ireland) and R. Lannigan. 1969. Auto-immune nephritis in rats. J. Pathol. 97:537-543.

Autoimmune nephritis was induced in black-and-white hooded rats by repeated intraperitoneal injections of a Wistar rat renal tubular preparation in complete Freund's adjuvant. The rat lesions on light-, electron-, and fluorescence-microscopy are similar to the lesions of idiopathic membranous glomerulonephritis in man. The pathogenesis of the experimental disease is discussed. - *M.J.A.*

83. Bernstine, R. L. (Experimental Surgery Division, Clinical Investigation Department, Naval Medical Research Institute, National Naval Medical Center, Bethesda, Maryland 20014). 1970. A chronic renal model for the fetus. Lab. Anim. Care 20:949-956.

The preoperative preparations of the ewe were discussed, including diet restrictions, preparation of the operative site, premedication, and anesthesia. The urinary bladder was selected as the access site to the fetus on the basis of anatomic and surgical considerations. The surgical procedure of inserting a catheter into the fetal urinary bladder together with the potential pitfalls was presented. Postoperative management was discussed in detail, including the rationale for each procedure. The renal function of the sheep fetus was determined for 2 gestational periods of 108-125 days and 126-142 days. Urine flow was not changed in the 2 periods of gestation. A decrease was noted in urinary sodium excretion as term approached. A slight decrease in potassium excretion was observed in the older fetuses; chloride excretion remained relatively unchanged. Creatinine excretion increased with progression of the pregnancy. The fetuses were sacrificed at periods up to 10 days following surgery to verify the absence of pathologic changes on the fetal urinary tract subsequent to the surgical procedure. - *Author's summary.*

84. Burrous, S. E. (Eaton Laboratories, Norwich Pharmacal Company, Norwich, New York 13815), and J. B. Cawein. 1969. Rat pyelonephritis model suitable for primary or secondary screening. Appl. Microbiol. 18:448-451.

A rat Proteus and Escherichia pyelonephritis model is described in which reproducible chronic infections are achieved and the efficacy of clinically effective agents is reliably demonstrable with five rats in 17 days. It can serve as a primary screen in which one technician can evaluate 180 compounds per month with 900 rats. The manner of inoculation will inherently allow the study of and distinction between metabolism which is peculiar to infection and that which is characteristic of trauma and healing in general for the elucidation of chemical correlations with effective therapy. - *Authors' abstract.*

85. Christen, P. (Biophysics Research Laboratory, Department of Biological Chemistry, Harvard Medical School, Boston, Massachusetts), W. C. Peacock, A. E. Christen, and W. E. C. Wacker. 1970. Urate oxidase in primate phylogenesis. *Europ. J. Biochem.* 12:3-5.

Several genera of New World monkeys have high uric acid concentrations in serum and urine comparable to man and the higher apes. Like man these animals lack urate oxidase activity in liver tissue. The purine metabolism of these non-human primates appears to be similar to that of man as exemplified by fasting-induced hyperuricemia. These South American monkeys should provide an easily accessible experimental system for the study of purine metabolism in a species closely related to man. Old World monkeys and prosimians have low uric acid concentrations in serum and urine. The urate oxidase activity of prosimian liver is remarkably stable whereas that of Old World monkeys was found to be quite unstable, a probable reflection of the gradual degeneration of this enzyme in primate phylogenesis. These non-human primates should serve as invaluable experimental subjects for studies of the regulation of purine synthesis, and the renal excretion of urate, processes which are impaired in human disease such as gout of the X-linked hyperuricemia syndrome. Moreover, access to these readily available experimental animals should provide the opportunity to study the effects of nutrition, electrolyte alterations and drugs on purine metabolism in a species closely related to man. Finally, it is not unreasonable to expect that diseases corresponding either to gout or to the X-linked hyperuricemia syndrome will be found to exist in these species providing an ideal experimental system for the study of abnormal purine metabolism. - *Authors' abstract modified.*

86. Gleiser, C. A. (Laboratory Animal Resources Center, Department of Veterinary Public Health, College of Veterinary Medicine, Texas A&M University, College Station, Texas 77843), G. L. Van Hoosier, and W. G. Sheldon. 1970. A polycystic disease of hamsters in a closed colony. *Lab. Anim. Care* 20:923-929.

A polycystic disease of hamsters was described. This entity was manifested by the presence of true cysts in the liver, epididymis, ovary, and adrenal, and cystic dilatations of the seminal vesicles, renal pelvis, endometrium, pancreas, and esophagus. Seventy-six percent of hamsters 13-27 months had cystic lesions, and 39% had cysts at multiple sites. These cysts vary in size considerably and were found in as many as 4 different sites in the same animal. This entity bears resemblance to congenital polycystic disease of man. - *Authors' summary.*

87. Johnson, W. J. (Food and Drug Research Laboratories, Department of National Health and Welfare, Tunney's Pasture, Ottawa, Canada), B. Stavric, and A. Chartrand. 1969. Uricase inhibition in the rat by s-trizines: An animal model for hyperuricemia and hyperuricosuria. Proc. Soc. Exp. Biol. Med. 131:8-12.

Oxonic acid and allantoxidine were potent in vivo inhibitors of uricase. Oxonic acid, when fed to rats or injected intraperitoneally, produced a marked increase in blood plasma urate levels and urinary uric acid output with a concomitant decrease in urinary allantoin excretion. Addition of 5% oxonic acid plus 1% uric acid to the diet resulted in a 22-fold increase in urinary uric acid by day 23 of treatment with deposition of uric acid in the kidney tubules. The oxonic acid-treated rat may serve as a useful animal model for the study of hyperuricemia and hyperuricosuria. - *Authors' summary.*

88. Kim, H. L. (The Highlands Clinic, P. O. Box 681, Williamson, West Virginia 25661), P. C. Labay, S. Boyarsky, and J. F. Glenn. 1970. An experimental model of ureteral colic. J. Urol. 104:390-394.

A satisfactory experimental model for the in vivo study of ureteral colic and passage of ureteral calculi has been developed utilizing the mongrel dog as the animal model. While the many factors involved in ureteral colic and influencing passage of ureteral calculi cannot be evaluated fully in this experimental model, the significance of hydrostatic pressure, ureteral dilatation, mucosal response and peristalsis can be assessed. - *Authors' summary modified.*

89. Safouh, M. (Department of Pediatrics, University of California at Los Angeles, Los Angeles, California 90024), J. F. S. Crocker, and R. L. Vernier. 1970. Experimental cystic disease of the kidney. Sequential, functional, and morphologic studies. Lab. Invest. 23:392-400.

This study evaluated the cystic kidney disease resulting from the long term feeding of diphenylamine in the diet of 120 Sprague-Dawley rats as (1) 2-1/2, (2) 1-1/2, and (3) 1-1/2 and 2-1/2 percent diphenylamine with 0.25 percent sulfur-containing amino acids. The concentrating ability of the rats was reduced before gross pathologic defects were discernible. Sulfur-containing amino acids significantly increased the degree of cystic changes. Analysis of urea and sodium in the papillary tip showed decreased urea concentration without significant changes in sodium concentration in rats with cystic disease. Serum potassium increased significantly with progression of the disease. Microdissection studies of cystic kidneys delineated the anatomical site of the defect as the collecting tubule. The possible relationship of this model of experimental cystic disease to cystic disease of the kidney in man is discussed. - *Authors' abstract.*

90. Stavric, B. (Food and Drug Research Laboratories, Department of National Health and Welfare, Ottawa, Canada), W. J. Johnson, and H. C. Grice. 1969. Uric acid nephropathy: An experimental model. Proc. Soc. Exp. Biol. Med. 130:512-516.

A nephropathy was experimentally induced in rats by feeding a diet containing uric acid and oxonic acid, a uricase inhibitor. It was characterized by

hyperuricemia, hyperuricosuria, deposition of uric acid in the kidney tubules, distention of tubular lumens, and early tubular and interstitial nephritis, and thus could serve as a useful experimental model for uric acid nephropathy. - *Authors' summary.*

91. Takeda, T (Department of Pathology, Chest Disease Research Institute, Kyoto University, Kyoto, Japan), and A. Grollman. 1970. Spontaneously occurring renal disease in the guinea pig. Amer. J. Pathol. 60:103-107.

Lesions appear spontaneously in guinea pigs of the Abyssinian and Hartley strains which resemble those of nephrosclerosis in the human being and differ from the spontaneously occurring and virus-induced nephritis previously observed in the mouse and rat. The lesions are not inhibited by immunosuppressant drugs (cyclophosphamide or cortisone) nor are they accompanied by bacterial infection of the kidney. The lesions progress with age and are apparently responsible for the gradual increase in systolic and diastolic blood pressure noted with increasing age. - *Authors' summary.*

92. Vosti, K. L. (Department of Medicine, Stanford University School of Medicine, Stanford, California 94305), L. H. Lindberg, J. C. Kosek, and S. Raffel. 1970. Experimental streptococcal glomerulonephritis: Longitudinal study of a laboratory model resembling human acute post-streptococcal glomerulonephritis. J. Infect. Dis. 122:249-259.

An experimental model of acute poststreptococcal glomerulonephritis is described. The experimental disease in rats was characterized by an early transient phase of minimal proteinuria which was not restricted to the nephritogenic strain, a latent period, and a secondary recrudescence of a much greater proteinuria only in animals exposed to the nephritogenic strain. This secondary phase of proteinuria developed shortly after the onset of measurable type-specific serum antibodies and at the same time that fixed gamma-globulins, streptococcal M protein, and beta-1-C globulins were first detected in the region of the basement membrane of the glomerulus. The gamma-globulins were eluted from the kidneys of these animals and reacted only with type 12 streptococcal M protein. These findings suggest that the secondary phase of proteinuria, which was restricted to the nephritogenic strain, is mediated by the fixation of complexes of type 12 streptococcal M protein and type-12-specific antibody in the region of the basement membrane of the glomerulus. In contrast, the early transient phase of proteinuria, which was not restricted to the nephritogenic strain, occurred in the absence of such immunologic changes and is presumed to reflect a toxic response to some cellular or extracellular product of the streptococcus. The resemblance of this model to a similar disease observed in man suggests that the same pathogenetic mechanisms may be operative. - *Authors' summary modified.*

BACTERIAL DISEASES

93. Sack, R. B. (Johns Hopkins University Center for Medical Research and Training, 4A Orient Row, Calcutta 17, India), and C. C. J. Carpenter. 1969. Experimental canine cholera. I. Development of the model. J. Infect. Dis. 119:138-149.

An experimental canine model has been developed in which a syndrome closely resembling human cholera can predictably be produced. Following an inoculum of a 5-6 hour culture containing 10^{11} vibrios, and an incubation period of less than 18 hours, 40% of dogs developed vomiting and massive watery diarrhea leading to severe depletion of fluid and electrolytes, acidosis, and death. Untreated, the disease ended fatally in 90% of these dogs, usually within 24 hours, at which time an average of 12% of body weight had been lost in diarrheal fluid. With adequate intravenous therapy, the disease lasted about 36 hours, during which time average stool losses amounted to 37% of body weight. The disease was found to be secondary to local proliferation of vibrios within the small-bowel lumen; no mucosal damage was recognizable. High concentrations of vibrios were found in the stool during acute illness. Vibrios were excreted in the stool for less than 1 week, and following recovery no sequelae were found. -

Authors' summary.

94. Vaidya, M. C. (Department of Human Anatomy, University of Oxford, Oxford, England), E. Palmer, G. Weddell, and R. J. W. Rees. 1970. A note on the presence of *Mycobacterium leprae* in the central nervous system of a mouse with lepromatous leprosy. J. Med. Microbiol. 3:194-196.

Results of histopathological study of the tissues of a mouse experimentally infected with *Mycobacterium leprae* indicate that leprosy bacilli can cross the blood-brain barrier and multiply in the brain and that they gain access to ganglion cells by a haematogenous route. The findings are discussed with reference to lepromatous leprosy in man and the use of the thymectomised irradiated mouse as a model for the study of the disease. - *Authors' summary.*

FUNGAL DISEASES

95. Brown, J. R., and F. von Lichtenberg (Department of Pathology, Peter Bent Brigham Hospital, 721 Huntington Ave., Boston, Mass. 02115). 1970. Experimental actinomycosis in mice. Study of pathogenesis. Arch. Pathol. 90:391-402.

Actinomyces israeli produced infection in 93% of inoculated mice. Roughness of strain and age of mice were important factors leading to infection. Abscesses which formed by one week slowly increased in size and persisted for eight months. Lesions resembled natural actinomycosis, except that fistulae did not form. Within the abscesses the colonies of organisms (granules) developed eosinophilic fringes which contained protein, but no neutral polysaccharide. New granules and abscess loculations formed during the course of the chronic infection. A hitherto undescribed "hyaloid" material appeared in the lesions but its origin is unknown. The histopathology and evolution of experimental actinomycosis as a model of chronic suppurative infection are described. - *Authors' abstract.*

96. Landay, M. E. (Clinical Laboratories, Jewish Hospital, Cincinnati, Ohio 45229), J. Mitten, and J. Millar. 1970. Disseminated blastomycosis in hamsters. II. Effect of sex on susceptibility. Mycopath. Mycol. Appl. 42:73-80.

This work was undertaken to study facts pertaining to the difference in susceptibility of male and female hamsters to blastomycosis. Female hamsters were more resistant than males to the lethal effects of infection with Blastomyces dermatitis. Ovariectomy increased the resistance of females, and castration increased the resistance of males. The clinical features of the disease in hamsters following intramuscular infection was contrasted with primary cutaneous blastomycosis and disseminated blastomycosis in humans. Although disseminated blastomycosis in hamsters does not resemble the human disease in all respects, there appear to be enough similarities to suggest the hamster as an excellent model for the study of the disease in humans. - M.J.A.

NUTRITIONAL-METABOLIC DISEASES

97. Barth, W. F. (Arthritis Division, Department of Medicine, University of Maryland, School of Medicine, Baltimore, Maryland 21201), J. T. Willerson, R. Asofsky, J. N. Sheagren and S. M. Wolff. 1969. Experimental murine amyloid. III. Amyloidosis induced with endotoxins. Arthrit. Rheum. 12:615-626.

A new model for the study of experimental amyloid is described using parenteral administration of endotoxin. The differential responses in the various strains of mice examined suggested that genetic factors may be involved in murine amyloid formation. Many similarities were noted between casein- and endotoxin induced amyloidosis. It is suggested that endotoxin may be involved in the pathogenesis of several forms of experimental amyloidosis. - *Authors' abstract.*

98. Cornelius, E. A. (Yale University, School of Medicine, New Haven, Connecticut). 1970. Amyloidosis and renal papillary necrosis in male hybrid mice. Amer. J. Pathol. 59:317-326.

Female SJL/J mice were mated with male (A x C57BL/1)F₁ hybrid mice. The offspring, SJL/J x (A x C57BL/1), were observed over a 13-month period, during which time a high mortality was observed in males. Post mortem examination of 20 males and 20 females showed a 95% incidence of severe amyloidosis of the kidney, spleen and liver, plus renal papillary necrosis in males, and a much lower incidence of mild amyloidosis without papillary necrosis in females. Histologic study of SJL/J, A, C57BL/1 and (A x C57BL/1)F₁ controls showed a high incidence of amyloidosis and renal disease in the A strain, and a lower incidence of amyloidosis in the SJL/J strain. Amyloidosis in controls was much less severe than that in SJL/J x (A x C57BL/1) males; there was no strong sex-linked relationship. Since there was no evidence of chronic disease, the high incidence of amyloidosis in SJL/J x (A x C57BL/1) males appeared to be due to genetic factors. It is suggested that hybrids of the S/J and A strains may be useful models for intensive study of the relationship of amyloidosis, aging and immune processes, especially in relation to renal function. - *Author's Abstract.*

99. Ellis, F. W. (Department of Pharmacology, University of North Carolina School of Medicine, Chapel Hill, North Carolina 27514), and J. R. Pick. 1970. Experimentally induced ethanol dependence in rhesus monkeys. Exp. Therapeut. 175:88-93.

The experimental induction of an apparent state of physiologic dependence on ethanol has been achieved in rhesus monkeys by the maintenance of relatively short periods of chronic ethanol intoxication. Animals were given 4 to 8 g/kg of ethanol (25% w/v) by gastric intubation in two or three fractional daily doses. In general, the blood-ethanol concentration fluctuated during 24-hour cycles over the range of 100 to 500 mg/100 ml, resulting in varying levels of intoxication. Termination of ethanol administration after 10 to 18 days of treatment resulted in the emergence, during the withdrawal periods, of a series of hyperexcitability signs which could be classified into tremulous, spastic and convulsive stages. The progressive severity of these stages could be correlated with declining blood-ethanol concentration. The convulsive threshold was reached prior to the complete disposal of ethanol. Both mild and severe abstinence reactions could be suppressed by ethanol administration. Signs in surviving animals that were untreated during withdrawal gradually subsided within 2 to 3 days and thereafter these monkeys apparently reverted to normal states of behavior and neuromuscular tone. These observations suggest that an animal model of the biologic component of experimental alcoholism was induced in the rhesus monkey by this regimen of treatment. -
Authors' abstract.

100. Fredrickson, D. S. (Molecular Disease Branch, National Heart Institute, National Institutes of Health, Bethesda, Maryland 20014), H. R. Sloan, and C. T. Hansen. 1969. Lipid abnormalities in foam cell reticulosis of mice, an analogue of human sphingomyelin lipidosis. J. Lipid Res. 10:288-293.

The lipid changes in the inheritable foam cell reticulosis of mice discovered by Lyons, Hulse, and Rowe have been reexamined. The major abnormality in thymuses from homozygous-abnormal animals has been identified as an increase in the concentration (per milligram of protein) of sphingomyelin and cholesterol. This increase is associated with normal sphingomyelin-cleaving activity. The lipid compositions of the liver and spleen in the homozygous-abnormal animal and of the thymus in the heterozygous-abnormal mouse are normal. The disorder appears to be chemically analogous to those forms of human sphingomyelin lipidosis (Niemann-Pick disease) that are not accompanied by a decrease in tissue sphingomyelinase. -
Authors' abstract.

101. Kramer, H. J., and H. C. Gonick (Department of Medicine, University of California at Los Angeles, School of Medicine, Los Angeles, California 90024). 1970. Experimental Fanconi syndrome. I. Effect of maleic acid on renal cortical Na-K-ATPase activity and ATP levels. J. Lab. Clin. Med. 76:799-808.

The injection of maleic acid into dogs or rats is known to produce a generalized defect of renal tubular transport similar to the congenital or acquired Fanconi syndrome. The present study has investigated the roles of the transport enzyme sodium and potassium-activated adenosine triphosphatase (Na-K-ATPase) and its substrate adenosine triphosphate (ATP) in this experimental model. Two groups of female Sprague-Dawley rats were injected intraperitoneally with maleic acid (1.5 or 9.0 mmole per kilogram of body weight). An immediate diuresis, natriuresis, glucosuria, and increase in urinary pH occurred in both groups of animals. One hour after injection, renal cortical Na-K-ATPase activity was inhibited 33 per cent in the 1.5 mM group and 41 per cent in the 9.0 mM groups,

while ATP concentrations were reduced 31 and 87 per cent, respectively. In vitro studies confirmed that maleic acid was a potent inhibitor of renal Na-K-ATPase. These results indicate that the tubular transport defect produced by maleic acid is due both to impairment of cell metabolism (generation of ATP) and to inhibition of Na-K-ATPase. - *Authors' abstract.*

102. Luse, S. A. (Department of Anatomy, College of Physicians and Surgeons of Columbia University, New York, New York), A. Rhys, and R. Lessey. 1970. Effects of maternal phenylketonuria on the rat fetus. *Amer. J. Obstet. Gynecol.* 108:387-390.

In chronically phenylketonuric rats, delayed intrauterine development was observed in spite of prolongation of gestation by 1 to 3 days. Bilateral cataracts (7 of 24 fetuses) and fetal resorption also were observed. These findings are in keeping with the high incidence of abortion, malformation, and mental retardation among the nonphenylketonuric offspring of phenylketonuric mothers. The phenylalanine level of both human and animal fetuses has been shown to be 2 to 6 times greater than that of the phenylketonuric mother, apparently due to active transport of amino acids by the placenta. It is suggested that the elevated level of phenylalanine in intrauterine life is especially disastrous due to the lack of an adequate blood-brain barrier in the embryo. - *Authors' abstract.*

103. San Martin De Viale, L. C. (Facultad de Ciencias Exactas y Naturales, Universidad, Buenos Aires, Argentina), A. A. Viale, S. Nacht, and M. Grinstein. 1970. Experimental porphyria induced in rats by hexachlorobenzene: A study of the porphyrins excreted by urine. *Clin. Chim. Acta* 28:13-23.

Severe porphyria was induced and maintained for several months in rats by means of daily hexachlorobenzene administration via stomach tube. Urinary porphyrins with 8-, 7-, 6-, 5-, and 4-COOH were isolated and studied by column and paper chromatographic techniques, both qualitative and quantitative, and their absorption spectra and melting points were determined. The relative excretory pattern was: Uroporphyrin > coproporphyrin > phyriaporphyrin > 5-COOH porphyrin > 6-COOH porphyrin. By chemical decarboxylation, all these porphyrins were found to be the type III isomer with only traces of uroporphyrin I and 5-COOH porphyrin I. The predominant porphyrins in the liver were uroporphyrin III and phyriaporphyrin. These findings were compared with those reported in humans intoxicated with the same chemical and with those in patients with hepatic porphyria cutanea tarda. The main differences among these groups were in the isomeric composition of the uroporphyrin, 5-COOH porphyrin and coproporphyrin. Porphyria induced in rats by hexachlorobenzene appears to provide a useful experimental approach for the study of the metabolic changes involved in human porphyria. - *Authors' abstract.*

TERATOLOGY

104. Davis, S. D. (Department of Pediatrics, University of Washington School of Medicine, Seattle, Washington 98105), T. Nelson, and T. H. Shepard. 1970. Teratogenicity of vitamin B₆ deficiency: Omphalocele, skeletal and neural defects, and splenic hypoplasia. *Science* 169:1329-1330.

Vitamin B₆ deficiency was induced in pregnant rats with a deficient diet and with 4-deoxypridoxine, a B₆ antagonist. Treated animals developed typical skin changes of B₆ deficiency. Fetuses were small and appeared anemic. Major fetal malformations were omphalocele, exencephaly, cleft palate, micrognathia, digital defects, and splenic hypoplasia. This teratologic system was developed as a model for human syndromes that exhibit combined immunologic and neurologic or skeletal defects. - *Authors' abstract.*

105. Elizan, T. S. (Laboratory of Neurovirology, Department of Neurology, The Mount Sinai School of Medicine, New York, New York), and A. Fabiyi. 1970. Congenital and neonatal anomalies linked with viral infections in experimental animals. Amer. J. Obstet. Gynecol. 106:147-165.

This paper is a review of the significant literature on viral teratology in experimental animals. Twenty-three viruses have been reviewed for their ability to affect the developing embryo, fetus, or neonate of man and/or experimental animal models. The paper contains a table that summarizes the results of experimental work referred to in the report. - *M.J.A.*

TOXICOLOGY

106. Vogel, F., and G. Rohrborn (eds.). 1970. Chemical mutagenesis in mammals and man. Springer-Verlag: Berlin, Heidelberg, New York. 570 pp.

Many chemicals consumed by human beings have been found to produce mutations in tests with experimental animals. It has to be determined whether and under what conditions these compounds produce mutations in mammals, and hence to what extent they represent a danger to man. In a total of 30 articles by 24 authors, the first three define the problem; this is followed by descriptions of suitable mammalian test systems. The results of experiments with various groups of chemicals (cytostatics, acridines, caffeine) are then discussed. Statistical analyses of human populations provide a transition to the practical considerations of mutagenesis as such. - *Publisher's abstract.*

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